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Peak Trailing Limb Angle and Propulsion Symmetry in Individuals with Below Knee Amputation

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Dedication

I dedicate this work to my family, specifically my wonderful children and fantastic parents. I am proud to be a transition between your immense greatness. You inspire, challenge, and support me to be the greatest version of myself possible. I love you all.

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Background: Individuals with lower extremity amputation often present with kinematic and kinetic gait asymmetries and often have difficulty achieving symmetrical walking using their prescribed prosthesis. To understand the impact of limb loss on gait measures, studies often compare individuals with lower limb amputation to healthy control participants or compare the amputated limb to the uninvolved limb while completing a specified task like steady state walking. Commonly implemented treatments for individuals with lower limb amputation are based upon the assumption that equal use of both legs (symmetry) while completing bipedal tasks (e.g., walking) would be beneficial, matching the behavior seen in healthy control individuals. Underlying kinematic or kinetic symmetry, as well as a potential relationship of the two biomechanical gait variables in individuals with below knee amputation have not been thoroughly evaluated during steady state treadmill walking.

Methods: We explored potential underlying (a)symmetries in peak trailing limb angle (kinematic) and peak anterior ground reaction force (kinetic) in individuals with below knee amputation walking at self-selected walking speed on a treadmill without upper extremity support. We then implemented real-time visual feedback to alter symmetry and examine the potential relationship between peak trailing limb angle and peak anterior ground reaction force. Later, we recruited and tested healthy control individuals with and without a solid ankle foot orthosis (SAFO) walking at their self-selected walking speed on a treadmill and exposed them to a similar visual feedback program to alter their baseline (a)symmetry.

Population: We enrolled eleven of the planned twenty-four individuals with unilateral below knee amputation and fourteen healthy control participants without any lower extremity pathology or gait abnormality.

Results: We found that individuals with below knee amputation do have peak trailing limb and anterior ground reaction force asymmetries and unencumbered healthy control individuals demonstrate symmetry of the same outcome measures while walking on a treadmill at self-selected walking speed. The use of real time visual feedback yielded statistically significant differences in peak trailing limb angle in healthy control participants without a solid ankle foot orthosis ($p=0.04$), peak and impulse anterior ground reaction forces when wearing a solid ankle foot orthosis ($p=0.04$). Statistically significant correlation between peak trailing limb angle and peak anterior ground reaction force were found in individuals with below knee amputation at baseline ($p=0.0004$), with real time visual feedback for peak trailing limb angle ($p<0.0001$), and peak anterior ground reaction force ($p=0.0002$).

Conclusions: Real time visual feedback is one intervention used to alter walking symmetry. Our results do not demonstrate an overwhelming response to real time visual feedback by individuals with below knee amputation or their healthy control counterparts and should be interpreted with caution. This work does provide meaningful information for further studies and interventions to alter symmetry during steady state walking and begins to explore the potential relationship between peak trailing limb angel and peak anterior ground reaction force production during self-selected treadmill walking in individuals with below knee amputation as well as otherwise healthy control individuals.

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Abbreviations

%ST: Percentage of stance time.

AGRF: Anterior Ground Reaction Force

AP: Anterior posterior

BKA: Below Knee Amputee or Individual with Below Knee Amputation

COP: Center of Pressure

ESAR: Energy Store and Release

GRF: Ground Reaction Force

POF: Push-off Force

SAFO: Solid Ankle Foot Orthosis

SST: Single limb stance time

SACH: Solid Ankle Cushioned Heel

TLA: Trailing Limb Angle

VO_2: Volume of Oxygen Consumption

Chapter 1: Introduction

Introduction

Amputation or limb loss is a common and survivable occurrence that results in the loss of all or a portion of an extremity or appendage. Lower extremity amputation is the partial or complete loss or removal of one or both legs. This removal or loss can be due to traumatic or non-traumatic etiology. Whether due to a traumatic spontaneous event or non-traumatic planned intervention to save a portion of a viable limb, the consequences are often significant to the survivor. One of those consequences is an alteration in functional mobility or walking. General walking ability is widely varied following lower extremity amputation, and can range from non-ambulatory (i.e., wheelchair or bed bound) to nearly fully functional with a properly fitting prosthetic device[1,2]. Walking function in individuals with lower extremity amputation has different degrees of fall risk[3-9] and functional ability or limitation. Regardless of functional mobility status, an appreciable degree of gait asymmetry, generally defined as the unequal use of lower extremities to complete a functional task like walking, often persists when compared with similarly matched healthy controls[10-14]. These observed asymmetries may have functional consequences on activities, participation, and the overall health condition of the individual as described by the International Classification of Functioning, Disability and Health model[15,16]. The degree and impact of these observed asymmetries may be influenced by a variety of underlying individual/intrinsic, physical/performance, and prosthetic/device characteristics that can either contribute to or detract from successful ambulation. The relative impact of gait measure asymmetry among individuals with lower extremity amputation is highly dependent on the selected metric studied (e.g., step length, single leg stance time, vertical ground reaction force, anterior ground reaction force, secondary sequela (e.g., osteoarthritis, pain, joint degeneration), joint power, impulse, or work). Observable asymmetries are often a focus of clinical treatment by the physical therapist and prosthetist team when treating individuals with lower extremity amputation. However, the relationships of these asymmetries to one another and to other biomechanical measures of gait are not well understood. In addition, gait asymmetries can be highly variable across individuals with lower extremity limb loss, due in part to the individuals electing to use a variety of compensatory strategies to mitigate the impact of the loss of the lower extremity(ies). The level of amputation (below versus above the knee) and laterality (unilateral versus bilateral) of the amputation can further contribute to variability in gait function and (a)symmetry across individuals with lower extremity limb loss.

It is widely assumed that healthy, unencumbered, uninjured, adults walk with a reasonably symmetric (defined as equal or near equal use of both legs) gait pattern[17]. While there is some argument to the impact of limb dominance[17-20], unperturbed treadmill walking is generally seen as symmetric with some variance when walking at self-selected walking speed[17,20]. To evaluate the ability to alter or influence this assumed underlying symmetry in the healthy control adults, investigations have used visual feedback to alter their gait pattern, and then investigators have compared these results to baseline data for specific outcome measures[21-23]. Another approach used to investigate symmetry assumptions in healthy controls is to identify and restrict the primary source of the movement pattern. For example, to investigate the effects of a functional ankle/foot complex, a solid ankle foot orthosis (SAFO) can be used to restrict normal plantarflexion that generates propulsion. A SAFO also restricts tibial advance over the foot during stance, preventing normal ankle dorsiflexion resulting in early heel rise[24]. This may also result in compensatory effects in other joints throughout the lower extremity[24].

It is entirely possible, but not proven, that healthy control participants wearing an ankle foot orthosis might mimic individuals with below knee amputation[25,26]. Although not yet scientifically proven, limiting sagittal plane movement of the ankle in a similar manner and magnitude using two different methods might result in similar sagittal plane outcomes. Simply stated, the ankle power, plantarflexion joint moments, anterior or posterior ground reaction forces, etc. of the limb wearing a solid ankle foot orthosis in an otherwise healthy control individual, might resemble what is found in the amputated limb in the individual with a unilateral below knee amputation. We operate under this logical assumption because there have been no publications that directly measure healthy control individuals with SAFO against themselves with a below knee amputation. A variety of prosthetic feet with different mechanical characteristics are used by individuals with lower extremity amputation to generate propulsion or push-off force. None of the prosthetic feet commonly prescribed have demonstrated a full and complete replacement of the biological ankle in the otherwise healthy human adult. The only example that comes close to producing biological power output at the ankle, and thus directly impacting anterior ground reaction force or propulsion output is the powered ankle foot orthosis (BiOM) which produces approximately 2.4/kg compared to a normal average of approximately 3 W/kg[27]. The prosthetic foot attempts to replicate the foot in action and appearance. Similarly, a solid ankle foot orthosis, 'acts' as a non-biological device to replace motor control otherwise exhibited by the healthy adult. By limiting the active control or propulsive ability of the intact ankle/foot complex using a solid ankle foot orthosis, it is logical to believe that investigators can potentially approximate the effects of some the prescribed prosthetic feet commonly worn by individuals with below knee amputation[28]. However, this potential analog is not yet robust enough to make a definitive statement about the similarities between individuals with below knee amputation and healthy control individuals encumbered with a solid ankle foot orthosis. Within subject research study design does not have the ability to directly compare healthy control participants wearing a solid ankle foot orthosis to below knee amputation, as there is not a way to predict who will lose their lower extremity without already exhibiting significant gait deviations due to disease process or trauma. However, for some sagittal plane outcome variables related to propulsion, the impact appears to be potentially similar enough to proceed with a logical assumption that otherwise healthy individuals with a solid ankle foot orthosis, may closely enough mimic individuals with below knee amputation[10,25,29,30]. Interlimb asymmetry for anterior ground reaction force production in both individuals with below knee amputation and healthy control individuals wearing a solid ankle foot orthosis demonstrates a greater anterior ground reaction force produced in the intact limb when compared to the experimental limb[10,31]. This demonstrated asymmetry is indicative of a degree of relative impairment in the encumbered healthy individual that could be considered analogous to an individual with below knee amputation. Information on trailing limb angle of individuals with below knee amputation and health control participants wearing a solid ankle foot orthosis is not currently available for comparison. However, a very similar kinematic measure that should be considered is hip extension. Hip extension was found to be symmetric in the healthy control wearing a solid ankle foot orthosis when walking overground at self-selected walking speed[31]. Hip extension in individuals with below knee amputation have reportedly had slightly increased prosthetic leg hip extension when compared to the intact leg[6,32-34], To better understand these gait measures and their potential relationships, we investigated peak trailing limb angle symmetry and propulsion defined as peak anterior ground reaction force symmetry in individuals with below knee amputation, healthy control individuals, and the same healthy control individuals with a solid ankle foot orthosis (SAFO) using real time visual feedback while walking on a treadmill.

Trailing Limb Angle

Trailing limb angle is a spatial gait metric, defined as the angle created between a vertical line from the pelvis to the ground and a second line between the pelvis and the heel or center of the foot in terminal stance[35,36]. Like many gait variables, trailing limb angle is assumed to be symmetrical during steady state and straight-line walking in healthy control adults. It is also likely correlated with step length in healthy controls, as total step length is generated by the distance from the heel of the front foot to the heel of the trailing foot. This linear distance is generated by the angle of the right and left legs from the stable pelvis. The angle generated by the action of both legs during walking to create this linear distance is the sum of the trailing limb angle (angle created by a perpendicular line from the pelvis to the ground, and a second line from the pelvis to the trailing heel) and the angle generated by the of the forward leg (angle created by a perpendicular line to the ground and the heel of the forward limb), sometimes called limb advancement[13]. Trailing limb angle is relatively new and is yet to be used regularly in clinical practice to describe or measure gait function to describe gait deviations in clinical populations. Recently, a small number of research studies have investigated the magnitude of the trailing limb angle and found this metric to influence propulsion in stroke survivors[35-38]. When stroke survivors can better position the paretic trailing limb behind their pelvis (i.e., increase hip extension or trailing limb angle) it increases the ability for the limb to produce greater 'propulsion', as quantified by anterior ground reaction forces during terminal stance. It is unknown if individuals with lower extremity amputation present with a similar relationship between these two measures, or if they can even successfully adjust their trailing limb angle to influence propulsion like what has been described in stroke survivors. Similarly, it is unclear if restricting ankle motion in healthy controls will affect their ability to control and alter trailing limb angle or impact anterior ground reaction force production.

Anterior Ground Reaction Force

Anterior ground reaction force is commonly interpreted as the force generated by the body (typically by the lower extremities) in the anterior (forward) direction. This common interpretation is an explanation of biomechanical principles that describe how the body acts in its environment to produce a movement rather than the strict definition generated by physics and biomechanists. This force generation can translate into a forward movement of the body's center of mass during walking[35,37-43]. Anterior ground reaction force generation, or propulsion, has been linked to gait speed, insofar as increased propulsion relates directly to increased gait speed[44]. Gait speed is considered a very important indicator of function and has been coined the sixth vital sign[45,46]. Thus, the importance of sufficient anterior ground reaction force production is critical to the successful mobility and potential survival of individuals including those with lower extremity limb loss[45,46]. Individuals with lower extremity amputation (specifically below knee) have a reduction in prosthetic limb anterior ground reaction force production[6,47-49] when compared to the intact limb or healthy control counterparts. This results in an asymmetry of peak anterior ground reaction force generation, a kinetic measure of walking performance, in individuals with below knee amputation. This asymmetry, due to reduced force generation of the amputated limb, may have negative secondary consequences such as overuse of the intact limb to compensate[50,51]. It stands to reason that symmetric anterior ground reaction force is important for mobility and walking function, and the production of anterior ground reaction force may be related to trailing limb angle. To understand these two gait measures, and their potential relationship, a study incorporating real time visual feedback to alter the production of trailing limb angle or anterior ground reaction force with precise measurement is warranted.

Real Time Visual Feedback

Providing feedback to an individual patient or client with the goal of altering a behavior or movement patter is commonplace in physical therapy clinical practice. Biofeedback is a specific type of feedback that monitors and provides information to an individual for the purpose of learning a volitional physical function. This biofeedback often utilizes technology with sensors to provide visual, auditory, or tactile information to the user. Visual feedback implies that information is presented to the user in the context of something they can see and process that can occur synchronously (occurring immediately while the activity is being performed e.g. XBOX Kinect using motion sensing technology, Smart Balance Master® Force Platforms during standing activities with a screen to demonstrate weight bearing and center of pressure movement) or asynchronously (a visual representation of the activity is demonstrated after the event – e.g. reviewing a golf swing on video using swing analysis software, running, biking, or swimming movement analysis for endurance athletes). Synchronous or “Real Time” visual feedback is a type of biofeedback that has been used for the evaluation and treatment of many clinical presentations[14,21-23,52-71]. Real time visual feedback has previously been used to influence gait mechanics and mobility (e.g., stair climbing) in individuals with below knee amputation[14,53,54].

In physical therapy clinics, various types of feedback including visual feedback are frequently used to demonstrate an abnormal movement pattern(s) to patients/clients and encourage alteration of that movement towards a desired outcome. Ideal feedback is provided as quickly as possible to encourage alteration of an aberrant movement pattern. Real time visual feedback during treadmill walking is an example of this feedback as it provides feedback immediately to encourage alteration for the subsequent step and a review of the current or previous step. Individuals with lower extremity amputation have successfully used visual feedback of several gait measures and adjusted their gait patterns to achieve improved gait symmetry in alignment with the real time visual feedback provided[54]. Individuals with lower extremity amputation were found to have baseline asymmetries in push off force (POF), single support time (SST), and percentage of stance time (%ST). Interestingly all three metrics were found to have statistically significant reductions in asymmetry from baseline after a four (4) minute real-time visual feedback training program. Additionally, energetic consumption—measured by VO_2, heart rate and tidal volume—improved by 6%, 3%, and 22% respectively among all individuals with lower extremity amputation regardless of etiology, limb length, and type of amputation. Thus, it appears that individuals with lower extremity amputation can use visual feedback while walking to increase symmetry[53,54].

Symmetry

The feasibility and importance of gait symmetry is often disputed in lower limb loss research and treatment. It stands to reason that individuals missing all or some significant portion of a lower extremity should not be expected to exhibit equal use of the prosthetic or artificial limb which is made of various metals, foams, hydraulics, and man-made materials when compared to the uninvolved lower extremity with fully intact neuromuscular, somatosensory, skeletal, and vascular componentry capable of volitional and reflexive gross and fine motor movements capable of adjusting to intrinsic and extrinsic demands to accomplish a wide variety of tasks. Or simply stated, that a prosthesis does not currently have the ability to completely replicate a natural lower extremity and should not be expected to do so. It is argued that bipeds (e.g. humans) with major structural deficiencies in the neuromuscular skeletal system cannot demonstrate optimal (i.e. economical, efficient, and pain-free) and symmetric movement patterns[72], and some asymmetry may be unavoidable in cases of unilateral limb loss[10]. If symmetry seen in healthy normal gait is not possible, one might argue that the underlying (a)symmetry demonstrated by individuals with lower extremity amputation along with the impact of this (a)symmetry need to be better understood to maximize function in individuals with below knee amputation[73].

While perfect symmetry might be an unrealistic goal for individuals with lower extremity limb loss[73], the negative consequences of prolonged prosthesis is well documented[51]. Individuals with lower extremity amputation also clinically report wanting to 'look normal' when they are walking indicating a desire to mimic healthy normal walking without noticeable asymmetries. Thus, the clinical standard of care and patient centered treatment plan for the individual with unilateral lower limb amputation is often centered around minimizing gait asymmetries to maximize function and reduce complications or potential comorbidities associated with asymmetry or reduced mobility. In the absence of strong evidence or consensus of the 'ideal' level of (a)symmetry needed to maximize function for individuals with lower extremity amputation, especially individuals with below knee amputation in either trailing limb angle or anterior ground reaction force, we elected to implement a goal of symmetry in both peak trailing limb angle and peak anterior ground reaction force during treadmill walking.

Summary

Lower extremity amputation can be a life altering event with a variety of known and unknown secondary sequelae. While many individuals survive the amputation itself, the impact on walking outcomes has been well documented in the literature. As a group, individuals with lower extremity amputation demonstrate some asymmetries in gait measures, even with physical therapy or other clinical intervention. We selected two gait measures, peak trailing limb angle and peak anterior ground reaction force (i.e., propulsion) to better understand the impact of below knee amputation on symmetry during steady state, self-selected treadmill walking. Currently, trailing limb angle is rarely used in the clinical setting to describe an individual's gait pattern or impairment, but it has gained popularity as a potentially important gait measure to consider when describing the gait of clinical populations in research and practice. The relationship of trailing limb angle to propulsion (defined as peak anterior ground reaction force) has shown some promise in the literature as a viable relationship to potentially capitalize upon to improve walking function in stroke survivors, but it is not known if this relationship persists in individuals with below knee amputation. Propulsion is often linked to walking speed and thus overall functional health, indicating the need for mechanisms to improve and maintain this measure in individuals with below knee amputation. Both outcome measures are potentially impacted by the loss of a lower extremity, thus creating an underlying asymmetry during straight line steady state walking. To further understand the relationship of trailing limb angle and anterior ground reaction force, and the potential for individuals with lower extremity amputation to alter their underlying symmetry, similar analogous data collected could be collected in healthy controls with and without encumberment of the foot/ankle complex. It is unclear if and how the use of real time visual feedback can provide the necessary information to make a meaningful change in gait pattern symmetry in the otherwise healthy control adults and individuals with below knee amputation. Understanding the relationship between trailing limb angle and anterior ground reaction force is clinically meaningful because it is more feasible and reasonable for a practitioner to observe and provide feedback on trailing limb angle since measures of propulsion (anterior ground reaction force) are not visible without force plates.

In a series of experiments, we hoped to elucidate the relationship of trailing limb angle and propulsion (defined here as peak anterior ground reaction force[74]) during steady state walking. The selection of peak trailing limb angle and peak anterior ground reaction force as primary outcome measures was grounded in published literature on stroke survivors, potentially relating these two gait measures. We primarily focused on interlimb symmetry (comparing the intact against the impaired or encumbered limb) as current clinical practice and rehabilitation goals center around the recovery of function of the involved limb and achievement and demonstration of symmetric gait. First, we measured the ability to achieve or improve symmetry with real time visual feedback, and the potential impact of this symmetry on gait mechanics and selected outcome measures in individuals with below knee amputation. Next, we sought to strengthen our understanding of the potential relationship between peak trailing limb angle and peak anterior ground reaction force in otherwise healthy control adults. To investigate the mechanisms of altering symmetry in healthy control subjects we used real time visual feedback to encourage asymmetry in both peak trailing limb angle and peak anterior ground reaction forces during self-selected speed treadmill walking. Finally, we explored a potential analog to individuals with lower extremity amputation by investigating healthy control adults encumbered by a unilateral solid ankle foot orthosis. We used the same feedback paradigm provided to the individuals with below knee amputation to measure the ability to reduce baseline underlying gait asymmetries in encumbered healthy control adults.

Purpose

The purpose of this study was to investigate the potential relationship between peak trailing limb angle and peak anterior ground reaction force in individuals with below knee amputation and healthy control adults. The completion of this work provides a greater understanding of gait mechanics of individuals with below knee amputation as well as provides information about the use of real time visual feedback to alter either or both outcome variables. By understanding the potential for individuals with below knee amputation to use real time visual feedback to alter trailing limb angle or anterior ground reaction forces and the potential relationships we will begin to uncover potential treatment options for return to full walking ability and potentially a longitudinal reduction in secondary complications associated with lower extremity amputation. To complete this investigation, we completed a series of walking trials at individually determined self-selected walking speed with and without real time visual feedback. We designed a study paradigm for the use of real time visual feedback paradigm to 1) improve symmetry in individuals with below knee amputation, 2) worsen symmetry (increase asymmetry) in the unencumbered otherwise healthy control, and 3) improve symmetry in otherwise healthy control adults wearing a solid ankle foot orthosis.

During a series of treadmill walking trials, we collected kinematic and kinetic gait variables and used real time visual feedback to encourage desired gait behaviors determined a-priori. We followed a standardized data collection format with randomization of trial order based on outcome measure (peak trailing limb angle or peak anterior ground reaction force). We used the calculated average peak trailing limb angle and average peak anterior ground reaction force data collected during a baseline trial (Baseline) to familiarize participants with the use of real time visual feedback (Matched Trial). We then provided standardized instructions along with real time visual feedback to encourage outcome measure symmetry (Symmetry) or asymmetry (Asymmetry) based on the experiment (Figure 1).

Specific Aims

Aim 1: Quantify the effect of trailing limb angle visual feedback on gait symmetry measures in ambulatory individuals with below knee amputation.

> *Hypothesis 1: Visual feedback prescribing trailing limb angle symmetry will improve trailing limb angle symmetry.*
>
> *Hypothesis 2: Visual feedback prescribing trailing limb angle symmetry will improve anterior ground reaction force symmetry.*

Aim 2: Quantify the effect of anterior ground reaction force visual feedback on gait symmetry measures in ambulatory individuals with below knee amputation.

Hypothesis 1: Visual feedback prescribing anterior ground reaction force symmetry will improve anterior ground reaction force symmetry.

Hypothesis 2: Visual feedback prescribing anterior ground reaction force symmetry will improve trailing limb angle symmetry.

Aim 3: Investigate the relationship between anterior ground reaction force symmetry and trailing limb angle symmetry in individuals with below knee amputation.

Objective 1: Quantify the relationship between anterior ground reaction force symmetry and trailing limb angle symmetry when participants walk without visual feedback.

Objective 2: Quantify the relationship between anterior ground reaction force symmetry and trailing limb symmetry when prescribing trailing limb angle symmetry.

Objective 3: Quantify the relationship between anterior ground reaction force symmetry and trailing limb symmetry when prescribing anterior ground reaction force symmetry.

Aim 3 is exploratory and sought to understand the potential relationship between the two primary gait measures (peak trailing limb angle and peak anterior ground reaction force). This Aim was not powered for statistical analysis, but potential outcomes may be used to inform future investigations related to gait (a)symmetry in individuals with lower extremity amputation.

Quantify the effect of visual feedback on gait symmetry measures in healthy control individuals.

Hypothesis 1: Visual feedback prescribing anterior ground reaction force asymmetry will increase anterior ground reaction force asymmetry in the unencumbered healthy adult.

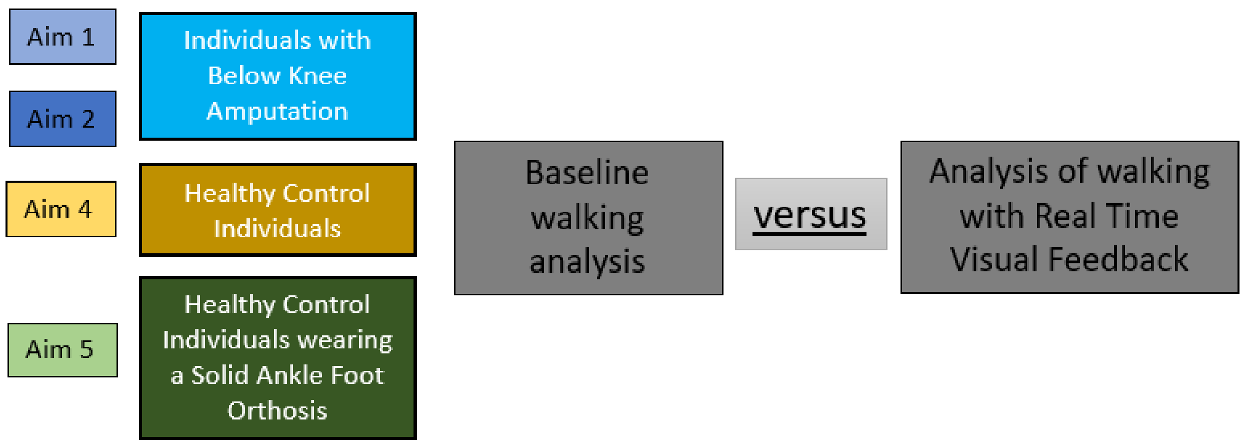
Hypothesis 2: Visual feedback prescribing peak trailing limb angle asymmetry will increase peak trailing limb angle asymmetry in the unencumbered healthy adult.

Aim 5: Quantify the effect of visual feedback on gait symmetry measures in healthy control individuals wearing a solid ankle foot orthosis.

Hypothesis 1: Visual feedback prescribing anterior ground reaction force symmetry will improve anterior ground reaction force symmetry in the healthy adult wearing a solid ankle foot orthosis.

Hypothesis 2: Visual feedback prescribing peak trailing limb angle symmetry will improve peak trailing limb angle symmetry in the healthy adult wearing a solid ankle foot orthosis.

Figure 1 Study Design: The study design will follow this general framework. Aims 1 and 2 are focused on individuals with below knee amputation while Aims 4 and 5 are focused on healthy control individuals with and without solid ankle foot orthosis, respectively. Aim 3 uses data collected from Aims 1 & 2 and is intentionally not demonstrated above. All trials and Aims are described in greater details below.



Chapter 2: Review of the Literature

Amputation Background

Amputation is defined as the removal of all or part of a limb and is clinically described by the etiology and level of the amputation. The terminology or classification of an individual as an 'amputee' is accepted among individuals with limb loss as acceptable 'person/patient/client first' language. Throughout this document we may use the terms interchangeably with permission from the patient population we studied. General classification and nomenclature often provide stereotypical information about mobility impairment, psychosocial adjustment, past medical history, for treatment planning, rehabilitation, recovery, and prosthetic device prescription. Amputation is a life-changing event that can result in depression, anxiety, body image disorders, psychological stress symptoms, and social discomfort[75,76]. Major amputation (sometimes also termed "limb loss" in clinical usage) is defined as amputation performed through or proximal to the tarsometatarsal joint[77] or loss of the fingers[77] of the lower and upper extremity respectively. The degree of severity of each amputation is influenced by secondary medical diagnoses (e.g., concurrent diabetes, Peripheral Artery Disease (PAD), metabolic disorder, etc.), and proximity of injury. For example, it is commonly held that an individual with an amputation at the tip of their toe is likely less severely affected (indicating reduced functional deficit and decreased need for rehabilitation services), than an individual that has had their entire leg amputated. This holds true for the upper extremity as well. The specifics of rehabilitation and prosthetic care vary across patients and settings, but a general framework of how amputations are approached is important to understand. Regardless of the etiology, limb amputation requires hospitalization, followed by rehabilitation and prosthetic fitting, and training. A variety of national and international clinical pathways contain many of these elements[78-80].

Amputation Incidence, Prevalence, and Cost

In 1996, an estimated 185,000 individuals underwent an amputation of the upper or lower extremity in the United States of America[81]. Lower extremity amputations specifically account for approximately 30,000-50,000 amputations per year[77]. Today it is estimated that there are 2 million Americans living with some form of amputation or limb loss[77]. These commonly cited estimates often do not include amputations that occur outside of private or public hospital systems and are only estimates based on databases or health systems. There have been no publications to date that include a registry or nationwide surveys to collect larger scale information on the incidence and prevalence of amputations in the United States. Despite these limitations in our knowledge, it is generally accepted that the incidence rate of amputations will likely continue to increase due to dangerous military conflicts (e.g., Operation Iraqi Freedom, Operation Enduring Freedom, and associated missions in the Afghanistan and Iraq theaters), and the epidemic of metabolic disorders and associated cardiovascular diseases. While these rates are likely to rise, survivorship from amputations is likely increasing as well due to improved surgical techniques. This increase in the number of individuals surviving with lower extremity amputation will require improved rehabilitation care and a team-based approach to optimizing movement through recovery and reducing secondary complications with prevention approaches. Lower extremity amputations have been estimated to have significant direct and indirect costs[82-84]. Annual total costs have been estimated at $8.3 billion in cumulative national hospital costs and up to $650,000 over the lifetime of the individual with lower extremity amputation[82,84,85]. Many of these costs do not represent the true cost to the individual because there has yet to be a study published that tracks individuals throughout the course of their lifetime. It can be expected that the overall costs are much greater, especially when reduced or lost productivity is accounted for in the analysis.

Amputation Etiology

The cause of amputation is traditionally broken into two primary classifications: Traumatic and non-traumatic. Traumatic amputations are associated with a sudden and unexpected event that results in the loss of part or all the limbs. These occurrences are typically outside of medical care and supervision and may result in death due to blood loss if action is not taken quickly. In contrast, a non-traumatic amputation can be due to chronic disease, cancer, or genetic malformation that necessitates the removal of all or part of the limb to enhance function or reduce the risk of secondary infection or complication. These non-traumatic amputations are typically scheduled medical procedures that could involve previous attempts to reverse the damage caused by disease or provide care to improve function to avoid limb removal. Regardless of the amputation etiology, all surviving individuals with lower extremity amputation receive medical treatment with a variety of outcomes possible based on the medical history, severity, motivation, and physical function of the individual. Rehabilitation and functional recovery of these two distinct groups may be different, thus research methodology must be clear in determining the population of interest.

Traumatic Amputation

Approximately 30,000 traumatic amputations occur each year[86]. In 2005, an estimated 45% of all amputations discharged from non-federalized hospitals in the United States of America were traumatic[77]. Traumatic amputations occur due to a variety of different causes but can be split into military or civilian categories.

Military Trauma

Active-duty traumatic amputation can be caused by explosions, penetrating, or crush injuries. These injuries may not occur in isolation if the event results in concomitant injuries like traumatic brain injuries or other musculoskeletal trauma. Amputations due to military trauma account for 10% or more of total US amputations and are not included in an estimate collected by Zeigler-Graham et al. in 2005[87,88]. These additional amputations are performed in Veterans Health Administration Hospitals and military hospitals either near the area of conflict or in the United States once the patient is stabilized. Amputations due to military injuries are typically not captured in large databases, because they occur in federalized hospitals or military bases. These hospitals are not represented in public health care databases and are not captured in systems level outcome data. Specialized research focused on veterans and service members in the United States must be separately incorporated into the scope of incidence and prevalence discussion.

Functional studies of these individuals tend to focus on return to full high-level physical function for potential return to service[89,90]. The number of individuals that seek a return to active duty after an amputation has increased from 2.3% to 16.5% during the 1980's[89] and it is reasonable to believe that number has risen given the nature of extended military conflicts as well as combatant weaponry resulting in increased amputations. However, a return to service is not guaranteed as many individuals with amputations have complicated medical cases that often do not pass the required fitness for duty assessments[91]. The Veterans Health Administration and Department of Defense have clinical practice guidelines to govern the treatment of limb loss survivors[79]. While these modules are helpful, they lack specific information on physical function and gait measures or metrics as benchmarks for progression through the continuum of care[79].

Military traumatic amputations differ from civilian traumatic amputations in that the baseline physical characteristics of the average American are different than that of service members. Service members undergo regular and routine physical challenges that could predispose them to an increased ability to recover full mobility with the use of a prosthetic device. Service members also participate in programs like the Comprehensive Soldier Fitness (CSF) program that is designed to increased psychological strength and positive performance to reduce the incidence of maladaptive responses[92-95].

Civilian Trauma

Civilian traumatic amputations are those that occur outside the line of duty and are treated at non-federalized facilities. Common causes for these civilian amputations are automobile or motorcycle accidents, workplace injuries, railway accidents, or severe burns[96,97]. Amputations due to motorcycle accidents result in more lower than upper extremity amputations (86.2% vs 13.8%), whereas amputations due to automobile accidents result in more upper than lower extremity amputation (54.5% vs. 45.5%)[86,97]. A study of the National Trauma Databank in 2010 found that men were more likely to have a traumatic amputation (77% vs 23%) with a mean age of 36 years old[97]. The exact cause could be a consequence of younger males engaging in risk-taking behavior like that seen in spinal cord injuries, but this has not been confirmed in the literature. Functional outcomes for each of these 'sub-etiologies' within the category of civilian trauma, has not been described in the literature but it is known that individuals post amputation must address coping mechanisms and psychosocial adjustment[98,99].

Non-Traumatic Amputations

Non-traumatic amputations make up the largest group of survivors with limb loss. It is estimated that nearly 55% of all amputations are due to diabetes or vascular disease[77]. Diabetes results from the inability of the body to produce and secrete sufficient insulin to breakdown and digest sugars in the body[100]. This results in abnormally high levels of sugar in the blood (glycemia). While often controlled with medication, individuals with diabetes often fail to maintain a healthy lifestyle and have complications leading to loss of vision, peripheral neuropathy, and amputation. The age adjusted rate of lower extremity amputation in diabetic population is approximately 15 times that of the non-diabetic population[101]. A 2009 estimate reported that 330/100,000 people diagnosed with diabetes will have a lower limb amputation at some point in their lifetime[102]. In 2006 there were approximately 65,700 amputations performed on individuals with diabetes[84,85]. Diabetes is a disease that impacts over 11 million individuals and is projected to balloon up to 29 million

Americans by 2050 using moderately increasing prevalence rates estimated based on 1998 data[101-103]. This would be a prevalence increase from 4.0% up to 7.2% from 1998-2050. Using a higher and potentially more accurate prevalence rate based on 1998 data, prevalence could be as high as 36 million[103]. A second leading cause of amputations is Peripheral artery disease (PAD) which appears to be even more dangerous and problematic. Between the years 2000-2008, approximately 186,000 individuals with PAD had a major lower extremity amputation. Peripheral artery disease is common in the elderly population with up to 50% of individuals over 85 years old with symptoms[104,105]. It is usually initially detected and assessed using the ankle brachial index, which indicates the level of stiffness and health of the arteries in the lower extremities. Amputations due to peripheral artery disease result in a staggering number of first-time amputations, but many of these individuals are at risk for subsequent amputations if the limb does not heal properly, or complete blood flow cannot be restored[85,106]. These individuals are also at risk once they have been fitted with a prosthesis if they have impaired sensation to the distal portion of the residual limb and are not compliant with limb and skin management. Non-traumatic etiology may also contain amputations that occur because of congenital abnormality and bone cancer. However, these two groups are often treated separately from other non-traumatic etiologies in reporting etiology statistics. For our purposes we will group them into the non-traumatic category for simplicity. A study from Denmark reported a 0.008/ per 10,000 persons amputation rate due to cancer between 1978 and 1987[107,108]. Congenital amputations have been observed at a rate of 3.8-5.3 per 10,000 births in the United States[107,109,110]. These numbers are low compared to the rates of the traditional traumatic and diabetic/vascular non-traumatic etiologies. [111]. Peripheral artery disease is common in the elderly population with up to 50% of individuals over 85 years old with symptoms[104,105]. It is usually initially detected and assessed using the ankle brachial index, which indicates the level of stiffness and health of the arteries in the lower extremities. Amputations due to peripheral artery disease result in a staggering number of first-time amputations, but many of these individuals are at risk for subsequent amputations if the limb does not heal properly, or complete blood flow cannot

be restored[85,106]. These individuals are also at risk once they have been fitted with a prosthesis if they have impaired sensation to the distal portion of the residual limb and are not compliant with limb and skin management. Non-traumatic etiology may also contain amputations that occur because of congenital abnormality and bone cancer. However, these two groups are often treated separately from other non-traumatic etiologies in reporting etiology statistics. For our purposes we will group them into the non-traumatic category for simplicity. A study from Denmark reported a 0.008/ per 10,000 persons amputation rate due to cancer between 1978 and 1987[107,108]. Congenital amputations have been observed at a rate of 3.8-5.3 per 10,000 births in the United States[107,109,110]. These numbers are low compared to the rates of the traditional traumatic and diabetic/vascular non-traumatic etiologies.

Demographics

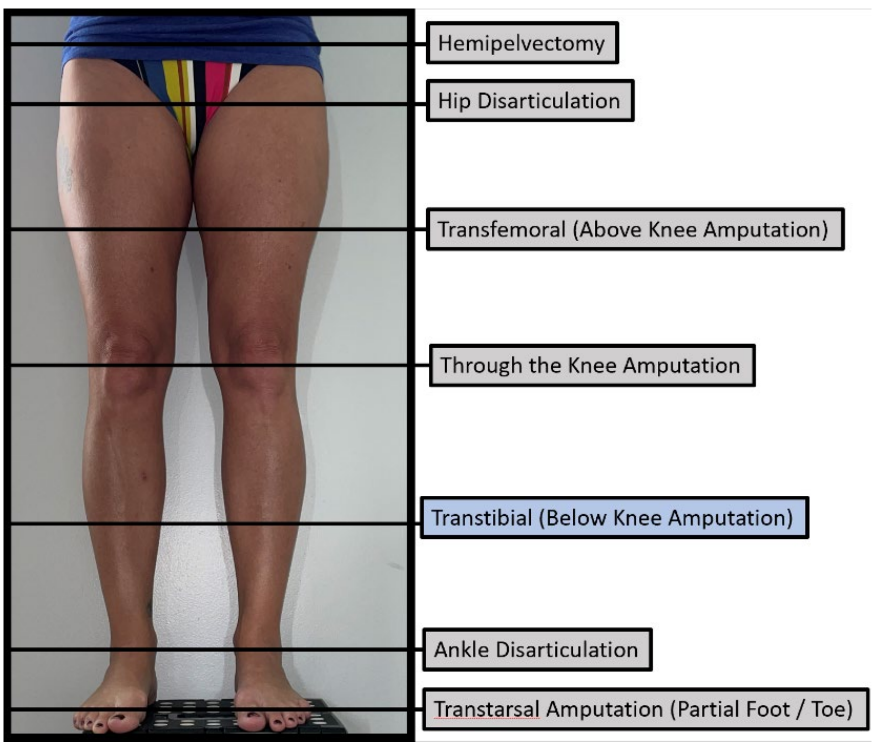
Age, gender, race, and socioeconomic status differences exist in various portions of the care and recovery of individuals with lower extremity amputation. For example, African-Americans are up to four times more likely to have an amputation than white Americans[112]. Individuals with lower socioeconomic status and reduced health literacy are at higher risk of amputation and complications due to chronic conditions[112]. Males are more likely to undergo amputation than females[113]. Limb salvage rates (a procedure that attempts to save the affected extremity using endovascular and similar procedures) are different among different race and ethnicity categories, with black/African American patients less likely than whites to undergo attempts to preserve the limb[113,114]. Individuals with advanced age are more likely to have amputations due to chronic conditions like diabetes and peripheral artery disease, children are more likely to have amputations due to congenital abnormalities, and young active males are more likely to have amputations due to trauma. The body of literature on these differences is expansive and is not the focus of this work. However, care should be taken to consider and appropriately address these factors when recruiting and analyzing data from individuals with lower extremity amputation.

Amputation level

Whether traumatic or non-traumatic, the functional effects of an amputation often vary depending on the type of injury sustained, as defined by the level. Amputations are classified on the level of the resulting surgery. Common levels for amputation are listed below (from proximal to distal)[115,116]:

<u>Lower Extremity[117]</u>: Hemipelvectomy / Hip disarticulations / Transfemoral (above the knee, AK or AKA) / Knee disarticulation (though the knee) / Transtibial (below the knee, BK or BKA) / Syme's amputation (through the ankle joint) / Partial foot or toe[117]. (See Figure 2) Each level of amputation results in distinct challenges to full functional mobility with different outcomes.

<u>Figure 2: Lower Extremity Levels of Amputation:</u> Individuals with lower extremity amputation are often classified by their level of amputation. Each level may have different functional difficulties and require unique rehabilitation intervention and prosthesis componentry.



Lower Extremity Amputation Gait Information

Introduction

Individuals with lower extremity amputation generally have a desire to return to normal unimpeded upright walking. Human bipedal walking requires the use of both lower extremities in a reciprocal pattern to move the center of mass in a desired direction. While recognizing that walking is a complex task that includes multidirectional stability and the ability to traverse different terrains, we will focus on the most basic form of locomotion; straight forward, steady state walking without an assistive device. Forward walking has been well described in the literature in healthy controls[118]. This framework serves as the baseline upon which we compare any pathologic gait abnormalities. In the case of individuals with lower extremity amputation, the physical loss of all or part of the lower extremity creates a unique challenge when understanding the interplay of the muscles and joints of the lower extremity on 'normal' gait mechanics.

A key measure of health and mortality is gait speed[119]. Reduced gait speed is associated with increased mortality and unfortunately, gait speed is reduced in individuals with lower extremity amputation population. Level of amputation directly impacts function. Individuals with above knee amputation have a slower walking velocity when compared to individuals with below knee amputation[120]. Etiology also impacts function. Individuals with amputation due to vascular causes have reduced gait speed when compared to non-vascular causes[121]. Gait speed is also related to activity and participation and has been tied to measures of falling. Speed is reduced in individuals with lower limb amputation classified as fallers when compared to non-fallers[121]. The impact of walking speed on gait mechanics is commonly accepted and has been demonstrated in the literature.

The study of gait can be broken down into three main areas: kinetic, kinematic, and spatiotemporal metrics. Kinetics, or the study of forces acting on the body while stationary or in motion (and the effects of these forces), can be measured using force plates either on a treadmill or on a walkway in three dimensions (anterior/posterior, medial/lateral, and vertical). While walking on a treadmill may be subjectively more difficult for the individual, kinetic measurements and calculation techniques can be considered largely similar to walking over ground[122-125]. Kinematics, or the study of motion, can be measured by tracking the body segments during walking, without reference to the forces that could produce the motion. Finally, spatiotemporal metrics deal with the distance and time portions of walking that result from the influence of the kinetics and kinematics. Spatiotemporal metrics are typically calculated by the position and time of each individual foot fall during walking. It is common to measure all three classes of gait metrics either on a treadmill or during overground walking. Early studies were not able to capture these data points on a treadmill, but recent advancements in technology allow for data collection on treadmills or using synced force plates in open laboratory spaces. It is important to note that while walking on a treadmill and overground may be similar in terms of output in healthy controls, individuals with pathology often self-report a fear of walking on a treadmill and increased difficulty which may alter any or all the measures collected.

Individuals with lower limb amputation have a variety of secondary complications as a result of losing all or part of their lower extremity. Here we will focus on individuals with below knee amputation to better understand the extent and direction of the changes on kinetic, kinematic, and spatiotemporal metrics during gait.

Kinetics

The study of gait kinetics describes the underlying mechanics that result in certain movement patterns[126]. Kinetics reflects the cause of movement described by forces, power, and energy[126]. Kinetics are not typically measured in clinical practice but are a staple of biomechanics research when describing human movement. Research has demonstrated differences when comparing individuals with lower extremity amputation to healthy controls as well as between the intact and impaired lower extremities.

Power

Power is defined as the rate of doing work and is calculated by dividing work by time or as the product of force by velocity. However, since we are analyzing human movement which largely occurs in an angular form around a joint, joint power is more commonly used. Joint power is the product of joint moment (or torque) and joint angular velocity or work/time[127]. Joint powers are calculated based on the combination of kinematic measures and ground reaction forces collected using force plates during walking, with calculations based on inverse dynamics. Traditionally joint powers have been calculated based on measures from static force plate(s) in the ground but advances in methodology and technology now allow for the use of treadmills with built in force plates for continuous data collection. In individuals with transtibial limb amputation, the loss of the ankle and foot logically impact the joint powers of the involved lower extremity.

Joint powers are often described with alphanumeric designation relating to the joint, and the burst number during the gait cycle. A full explanation of the power phases during gait can be found in a variety of publications but is best described by Winter seen in the left of the two side-by side figures below (labeled Figure 3 adapted from Winter)[72,118]. Essentially, each joint produces characteristic patterns of positive and negative power during the gait cycle. Borrowing directly from the publication, the accepted nomenclature of specific bursts of absorption and generation of energy are labelled and summarized as follows[72]:

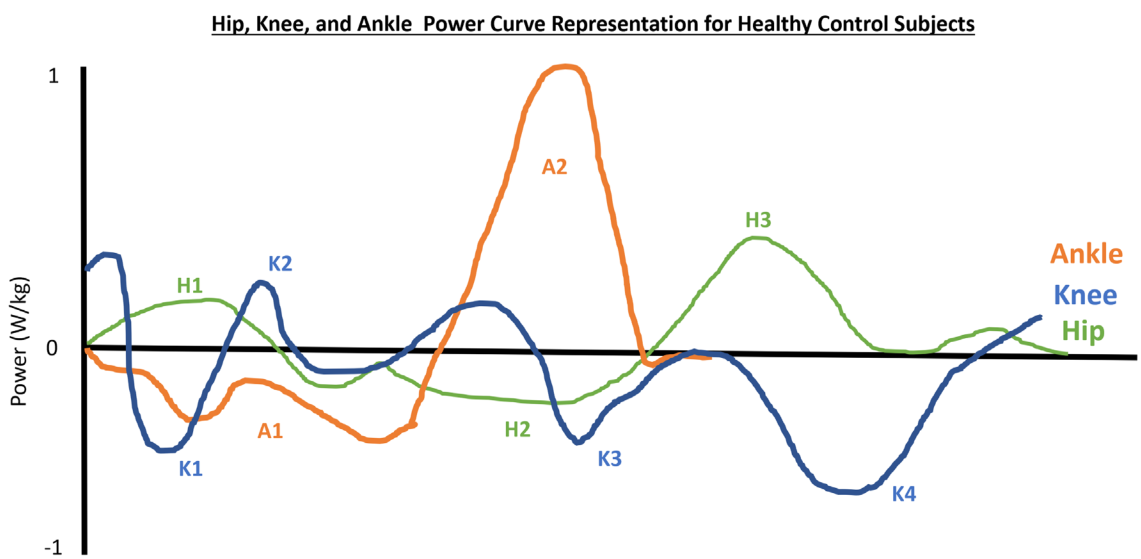
A1 – Absorption by plantar flexors as the leg rotates forward over flat foot.
A2 – Generation by plantar flexors (push-off) as the foot plantarflexes prior to toe-off
K1 – Absorption by knee extensors as the knee flexes during weight acceptance
K2 – Generation by knee extensors as the knee extends during mid stance to raise the center of gravity of the body
K3 – Absorption by knee extensors during push-off as the knee flexes prior to and after toe-off
K4 – Absorption by knee flexors at end of swing to take out energy of swinging leg and foot

H1 – Brief generation by hip extensors at weight acceptance as the hip extends (as knee flexes)

H2 – Absorption by hip flexors to decelerate backward rotating thigh

H3 – Generation by hip flexors as hip flexes before toe-off and in early swing to pull the lower limb upwards and forwards; this action is no referred to as pull-off (as opposed to push-off by the plantar flexors).

Figure 3: Lower Extremity Power Curves for Healthy Control Gait: Adapted from Winter et. al. (1998) hip, knee, and ankle joint power curves for the duration of the gait cycle for healthy control individuals. Major lower extremity joint power points are represented as H = Hip, K = Knee, A = Ankle and corresponding number in sequence during the gait cycle. These joint powers are subjects can change in magnitude and timing with alterations in speed or impairment/encumberment of either or both lower extremities.



<u>Figure 4: Lower Extremity Power Curves for Individuals with Below Knee Amputation Gait:</u> Adapted from Winter et. al (1998) demonstrates hip, knee, and ankle joint power curves for the gait cycle for individuals with below knee amputation. When compared to healthy control individuals, the timing and magnitude are different especially for the hip and ankle because of limb loss below the knee.

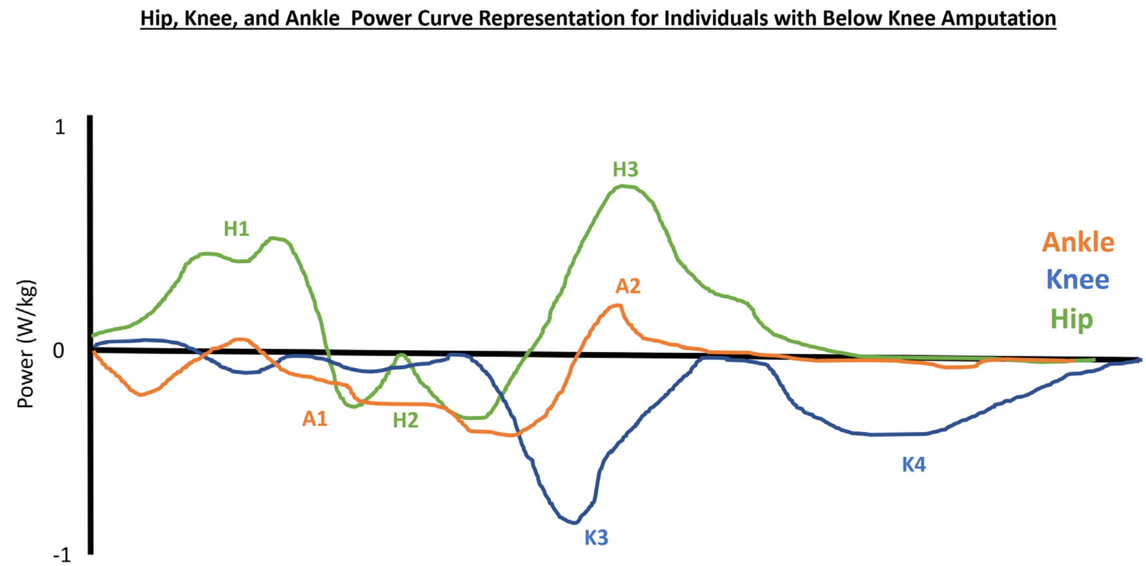


Figure 4 above demonstrates the power curves demonstrated by BKAs in the same Winter publication. Appreciable differences are noticed immediately with altered curve shapes and magnitudes. In healthy control gait, the plantar flexors are a major source of energy generation for push-off, while the knee extensors are major energy absorbers during early stance, and the hip plays a small and variable role in energy absorption and generation during early to mid stance[118,128]. The loss of the plantar flexors in individuals with lower extremity amputation requires compensation at other joints that contribute to energy production during walking. For example, the concentric activation of hip extensor musculature contributes to forward propulsion (or acceleration of the body's center of mass in an anterior direction) during early stance over the stance foot. The first power burst at the hip is commonly called the H1 power burst and is the result of hip musculature action during early stance. This H1 power burst likely involves concentric muscle contractions of the hip extensors, as the heel is on the ground and 'pulls' the body forward over the stance leg moving the hip from a flexed position into extension. The H1 power burst is seen in early stance and is completed by mid-stance and typically overlaps with the contralateral ankle plantarflexion during push off (A2) [72,118]. Through this action, the hip extensors are involved in trunk support and forward and upward propelling of the body's center of mass[129,130]. It is during this period that the hip extensors have the greatest impact on forward propulsion. Assuming the ankle plantar flexors are a primary group responsible for propulsion, it is reasonable to posit that the secondary group (hip extensors) would compensate for the loss of the ankle and foot. However, an individual with lower extremity amputation can elect to alter their gait in a variety of ways. If individuals are not able to generate enough force through the intact and prosthetic lower extremities for good quality gait, it is reasonable to suspect that their desire to walk will be reduced. This difficulty in achieving acceptable walking quality could lead to a reduction in walking activity (quantity). A reduction in walking quantity is directly related to secondary complications due to inactivity[131,132].

Hip Power

Increased hip power among individuals with lower extremity limb loss has been found in a variety of studies[74,128,133]. Prosthetic limb hip H1 power is increased above normal values when controlling for walking speed and is dependent upon the type of foot utilized during analysis[128]. Walking with traditional solid ankle cushioned heel (SACH) feet requires the highest mean hip extension power value, greater than Seattle and Flex feet. All values are 2-3 times that of normal hip extension power. The duration of the H1 power burst is also increased, lasting throughout the first half of stance (Percentage of stance phase that the H1 power burst is present: Healthy Controls 20%, Amputee 55-60%)[128,134,135]. This indicates that there is not only an increased magnitude of hip extension power, but also an increased duration of the power during stance phase. An above-normal energy generation during the H1 power phase has been reported in the prosthetic limb, suggesting compensation for the lack of energy generation by the ankle plantar flexors to move the body forward (i.e., forward walking). Between-limb hip power asymmetries are common in individuals with transtibial amputation, with higher peak H1 sagittal power in intact limbs than prosthetic limbs[133].

Ankle Power

The loss of a functional foot and ankle directly impacts the ability to produce joint powers at the involved limb. The prosthetic ankle has up to a 76% reduction in ankle power in the prosthetic leg when compared to the intact limb[135]. Prosthetic ankle A2 power burst is significantly less than in healthy controls[128]. Ankle power parameters are also greatly influenced by the type of prosthetic foot[133,136-138]. Solid ankle cushioned heel (SACH) feet demonstrate the lowest peak power compared to Seattle and Flex feet[128]. Energy storage and return feet commonly referred as ESAR or ESR only produce approximately 50% of peak plantarflexion power generated by an unimpaired ankle during powered plantarflexion[139]. Utilizing more advanced technology feet components (BiOM versus ESR) ankle power generation nearly doubles in the prosthetic limb and the asymmetry of ankle power between the intact and prosthetic lower extremity is reduced[139]. However, the increase in ankle power generation by the BiOM can exceed that normally seen in healthy controls as well as the intact lower extremity, creating a different type of asymmetry not otherwise seen in lower extremity limb loss gait. The between limb asymmetry remains for the ankle as it does for the hip. The loss of a functional foot and ankle directly impacts the ability to produce joint powers at the involved limb. The prosthetic ankle has up to a 76% reduction in ankle power in the prosthetic leg when compared to the intact limb[135].

Work

Work is defined as the product of force and distance (Work = F x D) and is reported in Newton*meters or Joules. In traditional mechanics, Work can be displayed graphically as the area under a force-position (or torque-angular position) curve[140]. Similarly, work can be illustrated as the area under a power-time curve, as is more common for gait mechanics. When discussing gait mechanics, work is described for a portion of the gait cycle like that seen with power. Positive work values represent energy generation in which a force is delivered in the same direction of the movement (e.g. concentric muscle contractions) and negative values represent energy absorption, or force generated in the direction opposite the movement (e.g. eccentric muscle contractions)[141]. Positive work at the proper phase in the gait cycle is often considered propulsion. Mechanical work can be a valuable metric because it is calculated in terms of the same measurement units as metabolic energy, allowing the calculation of "movement efficiency" measures – essentially the mechanical work that can be produced for a certain amount of metabolic energy. Joint work is altered in individuals with lower extremity limb loss. For individuals with unilateral transtibial amputation, knee total work during K1-K2 power phases (early stance phase) is greater in the intact limb, compared to prosthetic and control limbs[49,50,72,142-144].

In addition to the propulsion during early stance, the hip is also responsible for slowing down the progression of the trunk during initial contact and flexing the hip during swing. In unilateral BKA, hip total work during the H1 power phase in the intact limb was significantly increased compared to control limbs and displayed a particular pattern since it included initial negative work related to hip flexion[50]. The interaction of the negative and positive work in each hip produces characteristic movements that are described in the literature as step-to-step transition.

Moment

Joint moments have been used in the lower extremity limb loss population to characterize forward progression[134,144]. While individually important, they are less commonly used than power which includes joint moment in its calculation. Joint moments can be calculated for each lower extremity joint. Moments are calculated using inverse dynamics from ground reaction forces and angular kinematics at each joint. For individuals with lower extremity amputation, moments are commonly utilized but they have inherent variability due to calculation error[145]. When analyzing the gait of individuals with lower extremity limb loss there are some marked changes in joint moments at the hip during steady state walking when compared to able-bodied values[6,146,147], and both the residual and intact legs have greater hip extensor moments relative to non-amputees[50,74,128,148]. More specifically, hip extensor moments are greater during early stance in the intact lower extremity and prosthetic limb of individuals with transtibial amputation compared to able bodied controls, despite similar knee and hip angles throughout the gait cycle[147]. This indicates that both the residual and intact hips are working hard to compensate for the loss of the ankle.

Impulse

Hip extensor angular impulse quantifies the total contribution of the extensor moment to the movement carried out by integrating the time of the hip extensor moment during the H1 phase[50]. Values during the initial hip extension phase (H1) as well as during first negative power phase (H2) in both prosthetic and intact limb groups were similar and significantly higher than in the control group[50]. Interestingly, although the hip angular impulse values between the intact and prosthetic limbs were similar, the amount and timing of total work during H2 phase differed between prosthetic and intact limbs groups since total work was positive and negative, respectively[50]. Also, hip extensor angular impulse was found to be similar in individuals with transtibial amputation with different alignments of their prosthesis (normal, internal, and external rotation)[50].

Ground Reaction Forces

Ground reaction forces can be measured in three distinct but interrelated planes: Sagittal (anterior-posterior and vertical ground reaction force), and frontal (medial-lateral). During each footfall, an individual experiences forces in all three directions during the stance phase of gait. Ground reaction force measurements provide information on direction of force, timing, and magnitude. The vertical component typically describes the amount of loading on each limb, medial-lateral component provides insight about weight shifting, and anterior-posterior component describes propulsion and braking. Much of the focus in lower extremity limb loss gait research centers around vertical and anterior-posterior ground reaction forces.

Propulsion

Propulsion is commonly described in gait literature using kinetic variables: power; work; joint moment; and impulse[127,141]. The two most common are power and work. Propulsion during walking is a commonly accepted construct that generally refers to the ability of the lower extremities to accelerate the body (or body's center of mass) in a desired direction[38]. For our purposes we will consider only steady state propulsion in the anterior direction i.e., individuals walking forward at a constant speed. It is important to note that there is a growing body of literature that investigates changes during incline/decline, altered terrain, and stair climbing in individuals with lower extremity amputation. However, level ground, steady state walking arguably is the most studied condition and has the greatest functional relevance. Specific definitions of propulsion center around the forces or actions of the lower extremity to contribute to forward progression of the body[17,149]. Forward progression or propulsion can be defined by fore-aft accelerations of the body's center of mass[149]. This acceleration is generated in part by the muscles of the lower extremities acting across the joints to produce ground reaction forces at the body's interface with the walking surface. Propulsion has also been described as the combination of the hip and ankle moments developed at the end of the stance phase (final 50-60% of the gait cycle) where the lower limb propels itself forward[150]. The coordination of the hip and knee is critical for supporting the body against gravity and generation of movement to propel the body forward[150]. These lower extremity forces are calculated from ground reaction forces and are commonly labeled kinetic variables. Based on Winter's definitions of gait events, propulsion typically occurs during the second half of the stance phase for the plantar flexors and early stance for the hip extensors[127,149,151,152]. During BKA gait, ankle push-off is reduced, but the amount of reduction is related to prosthesis type[10,29,30]. How individual with lower extremity amputation overcome this loss of push-off is unclear. Several studies have aimed to identify compensations for this loss, but few have provided information on how individuals with amputation select their chosen compensation.

Vertical Ground Reaction Forces

Vertical ground reaction forces quantify how each lower extremity is being loaded. Ground reaction force data gives information about the force magnitude, raw and relative to body weight, and the duration of the stance phase – the portion of the gait cycle for which the leg is in contact with the ground. For individuals with lower extremity amputation, the intact limb bears a greater portion of the load during walking than the amputated limb[49,153,154], a pattern that is thought to lead to increased risk of secondary conditions such as increased risk of osteoarthritis[12], chronic low back pain[155], and degenerative joint changes[156]. Hip vertical ground reaction forces during gait are increased in individuals with lower extremity limb loss for the intact and prosthesis side compared to otherwise healthy control vertical contact forces[147]. Knee vertical contact force is increased on the prosthesis side, but not on the intact side[147]. This relationship is seen with a relatively consistent vertical ground reaction force in individuals with lower extremity limb loss and able body controls[147]. Peak vertical ground reaction force is significantly affected by a combination of independent factors of prosthesis, speed, and limb, but these independent factors may be within a range reported similar to healthy, able-bodied individuals[153].

Anterior ground reaction forces

Anterior ground reaction force is often used to quantify propulsion during gait. Two different metrics of the anterior ground reaction production are described in the literature: Peak or Impulse. Peak ground reaction force is quantified as the maximum anterior ground reaction force during a stride. This value can be normalized to the participants' bodyweight to account for inter-subject variability and is measured by a force plate during treadmill or overground walking. Impulse ground reaction force accounts for both anterior force magnitude and the duration of the gait cycle for which this anterior force is present. This can be calculated as the area under the curve when ground reaction forces are plotted against time. The use of impulse to describe anterior ground reaction force production has limitations especially when manipulating the gait cycle. Currently, there is no consensus for which definition of anterior ground reaction force should be used to describe propulsion in studies investigating gait mechanics of healthy control or individuals with below knee amputation.

The type of foot used by the individuals with lower extremity amputation (e.g., Solid Ankle Cushioned Heel (SACH) vs. Energy Store and Release (ESAR) vs. Powered foot)[136,138,157] may impact the anterior ground reaction force magnitude which could make conclusions less definitive. By design, the powered prosthetic foot produces plantarflexion torque during gait, whereas the solid ankle cushioned heel (SACH) foot has a fixed ankle and only varying degrees of 'cushion' as measured by the durometer of the cushioned heel. The ESAR is designed to improve walking performance in the individual with lower extremity limb loss requiring prosthesis by storing and releasing elastic energy during stance[158,159]. Due to its design and purpose, it is often a middle ground between the powered foot and SACH that provides some mechanical benefits, with reduced weight, power requirements, and price.

When investigating trailing limb angle and propulsion among stroke survivors or healthy control, some studies only report the peak ground reaction force values[36,37,160], others only report impulse ground reaction forces[161,162], while others elect to report both the peak and impulse ground reaction force values[41]. However, either or both anterior ground reaction force metrics are used in general gait studies focused on individuals with below knee amputation[6,163]. In our study we adopted peak anterior ground reaction force as the measure of propulsion as shown and used in previous studies[6,37,163].

In our study we primarily focused on peak anterior ground reaction force values for the intact and prosthetic limb for a few key reasons: 1) The feedback program utilized peak anterior ground reaction forces, 2) Peak is directly indicative of an increased magnitude of force generated during the push-off phase of the gait cycle without regard to the amount of time taken to generate the force, and 3) there is some evidence to suggest that peak is a better outcome measure than impulse with a much stronger correlation to walking speed especially when requesting the individual alter their gait pattern[160].

Kinematics

Kinematics are commonly reported at the ankle, knee, and hip when describing gait motion for healthy and clinical populations. Kinematic measures are typically near symmetric between the limbs in intact controls, but unilateral pathology results in changes within each limb.

Ankle

Ankle total range of motion in healthy control participants during gait averages 28 degrees[139]. The average ankle range of motion in individuals with lower extremity limb loss changes depending on the foot that is utilized both within participants (intact versus prosthetic) and between prosthetic foot design. Increased complexity of the prosthetic foot results in increased prosthetic range of motion (e.g. ESR: 20 degrees vs BiOM: 23 degrees)[139]. The solid ankle cushioned heel (SACH) foot has negligible ankle range of motion by design. The intact ankle of the individual with lower extremity amputation demonstrates increased ankle range of motion when compared to healthy controls(ESR: 20 vs ESR_{intact}: 33 degrees and BiOM: 23 vs $BiOM_{intact}$ 32 degrees)[139]. This indicates that the intact ankle of the amputated individual has greater range of motion compared to control values, and greater range of motion when compared to the prosthetic ankle[139].

Knee

Knee total range of motion in healthy controls is approximately 70 degrees during walking at self-selected walking speeds. Due to the alteration at the foot and ankle, individuals with lower extremity amputation often exhibit a reduced knee range of motion on the prosthetic side (ESR: 61 vs ESR_{intact}: 68 degrees and BiOM: 64 vs $BiOM_{intact}$ 68 degrees)[139]. The increase in foot prosthetic complexity with the BiOM likely contributes to the normalization of knee total range of motion evidenced by the smaller level of asymmetry between the legs.

Hip

Hip range of motion during steady state walking in healthy controls is approximately 40 degrees[139]. Even though the ankle and knee ranges of motion are altered in individuals with lower extremity amputation, hip range of motion is not significantly different from healthy controls in either the prosthetic or intact legs[139]. This similarity does not appear to be impacted by prosthetic foot and ankle[139] (ESR: 40, ESR_{intact} 39 and BiOM: 40, $BiOM_{intact}$:[53,139]). While the total hip range of motion thus appears approximately equal across these populations and legs, this measure does not account for potential differences in peak hip flexion and hip extension angles achieved while walking. With respect to these more detailed measures, hip extension during the stance phase appears to slightly increase in the prosthetic leg compared with the intact leg[6,32-34], but no significant differences are apparent in hip flexion angle[164]. These complex results prohibit us from identifying a single adaptation regarding hip kinematics following lower extremity amputation.

Spatiotemporal measures

Literature on spatiotemporal metrics is mixed for individuals with lower extremity limb loss. Increased spatiotemporal variability in step length and width as well as step and swing time has been found in individuals with transtibial amputation[165]. The non-amputated limb shows equal or greater average variability than the amputated limb[165]. However, when normalizing for gait speed, the variability of spatial measures decreases, while variability of temporal measures increases when compared to self-selected walking speed[165]. This is likely a result of individuals with lower extremity limb loss making small adjustments in spatial measures more than temporal features for adjusting walking speed[165]. There is a litany of commonly accepted spatiotemporal measures, but literature on limb loss gait focuses primarily on step length and single limb stance time as the spatial and temporal metrics, respectively.

Step Length (spatial measure)

Step length is the anteroposterior measurement from one heel to the opposite heel at initial contact. Specifically, prosthetic step length is measured from the heel of the intact limb to the heel of the prosthetic limb upon initial foot contact with the prosthetic limb. Intact step length is measured from the heel of the prosthetic foot to the heel of the intact foot upon initial foot contact with the intact limb. The two step lengths combined approximately equal the stride length. In normal healthy self-selected gait, it is assumed that the two step lengths provide equal contribution to the overall stride length; however, in pathologic gait, this assumption is often violated.

Prosthetic and intact limb step lengths demonstrate inconsistencies in individuals with below knee amputation [13]. It has been shown that these individuals may have a longer[11,120,166-171] or shorter[121,172,173] step length on the prosthetic side when compared to the intact limb. The reasons for this difference are unknown but may involve etiology, falls risk, and prosthetic componentry. For example, individuals with vascular disorders have a shorter prosthetic step length when compared to their non-vascular etiologycounterparts[121], increased fall risk shortens both prosthetic and intact step length when compared to non-fallers[121], and a powered prosthesis like the BiOM increases prosthetic step length[139]. Furthermore, deconstructing the step length into sub-components representing the trunk progression and forward foot placement demonstrates additional inconsistencies across individuals with lower extremity limb loss[13].

The single metric of step length may be flawed when interpreting the impact of a lower limb amputation[13]. Trunk progression asymmetry is impacted by speed manipulation with increased asymmetries noted at self-selected speeds over slow speeds[13]. Step length asymmetry was increased with slower speeds over self-selected speeds[13] and forward foot progression asymmetry is not impacted by speed manipulation[13].

Stance Time (temporal measure)

In individuals with below knee amputation, the stance phase is longer in the intact limb than the amputated limb[49,121,134,170,174-176]. The relative increased stance time on the intact limb corresponds to a reduced stance time on the amputated limb likely due to reduced balance confidence on the prosthesis or subjective discomfort of non-weight bearing structures becoming suddenly responsible for carrying the load of the entire body during the stance phase. Clinical treatment by a licensed physical therapy team incorporates balance training to improve the asymmetry commonly seen in individuals with lower extremity amputation and the implementation of a searing schedule and activity modification to improve standing and activity tolerance during waking hours while wearing the prescribed prosthesis.

Trailing Limb Angle and Propulsion Relationship

An emerging principle for pathologic gait is the concept of improving trailing limb angle to improve propulsion[35-38]. Trailing limb angle is defined as the maximum angle of the extended hip during terminal stance, (the position of the foot relative to the body center of mass at terminal stance)[35,36]. Trailing limb angle has been described as a component of step length[13] which has been shown to be a significant predictor and positively related to the propulsive impulse in the paretic, non-paretic, and control limbs in stroke survivors and healthy matched controls[35].

The investigation of trailing limb angle is motivated by the need to move beyond the simple measure of step length in defining spatiotemporal and kinematic (a)symmetry[13], as step length fails to account for potential individual differences in trunk progression and anterior foot placement. Quantifying trailing limb angle allows the investigation of individual limb positioning and the potential impact on propulsion. If the lower extremity is placed under the center of mass and a contraction of the ankle plantar flexors occurs, the force will be directed largely vertically and will not contribute to propulsion (defined as the progression of the center of mass forward). Positioning the foot more posteriorly when the generation of force is initiated at the ankle will increase the proportion of the force contributing to forward propulsion (assuming a rigid to semi-rigid strut at the knee). Thus, the position of the trailing limb when the force is generated is more important to propulsion than simple step length which includes the forward step position of the opposite foot in its calculation.

Trailing limb angle, anterior ground reaction force, and walking speed are all potentially interrelated. As walking speed increases, anterior ground reaction force[177], and step length (and thereby trailing limb angle) increase in healthy controls and individuals with lower extremity amputation[49]. It is not currently known if the relationship of trailing limb angle to anterior ground reaction forces when controlling for gait speed is present in individuals with lower extremity amputation. By understanding this relationship, further understanding of the ability of individuals with lower extremity amputation to achieve symmetric propulsion using kinematically similar patterns is reasonable (i.e., equal trailing limb angle producing equal amounts of propulsion comparing the intact and prosthetic lower extremity). This understanding of the relative contribution of trailing limb angle to propulsion in individuals with lower extremity amputation could also identify a degree of desired hip extension via trailing limb angle needed by the prosthesis compared to the intact lower extremity during steady state walking.

Symmetry

Individuals with lower extremity amputation have the ability to alter their symmetry given appropriate feedback. Previous studies prescribing feedback have limited symmetry training to four minutes, but there is little to no evidence that explains this amount of time or post training carry over[53,54]. However, there is one published example that utilizes feedback combining vertical and anteroposterior shear forces on individuals with either below or above knee amputation[53]. Individuals with transtibial amputation demonstrate altered hip and knee angle symmetry and timing of gait events with an increase in speed from self-selected to fastest-comfortable walking speed[176]. These changes were measured in three distinct phases of the gait cycle, and revealed reduced symmetry between the intact and prosthetic limb[176].

Among neurologically and orthopedically intact controls, common measures of gait mechanics are generally assumed to be near-symmetric during straight-line, steady-state walking. The presence of a clinical diagnosis has often been shown to alter walking symmetry. Individuals with lower extremity amputation are not immune to this alteration, even with the use of prosthetic limbs or components. Symmetry can be measured using a variety of measures in both healthy and clinical populations. Measures of symmetry in individuals with lower extremity amputation can be impacted by behaviors like altered walking speed[178-180] and can change throughout the rehabilitation process, as individuals with and without assistive devices demonstrate improved walking speed and symmetry during the first 75 days post amputation[14]. Increased speed may reduce asymmetries in the BKA[178].

Symmetry has also been investigated in vertical ground reaction forces and spatiotemporal metrics to determine the potential differences at increased speeds (0.5, 0.9, 1.2 m/s and maximum walking speed)[179]. Individuals with transtibial amputation produce greater peak vertical ground reaction force in their intact limb when compared to their prosthetic limb, and when compared to healthy controls. Walking speed affects the vertical ground reaction force of the intact limb to a greater extent than the prosthetic limb or healthy control limbs[179]. This demonstrates that kinetic asymmetry is not only present but is also able to change based on input and stimulus in individuals with lower extremity amputation.

Using a lower extremity ambulatory feedback system (LEAFS), a low-cost portable insole system that measure ground reaction forces in real time, symmetry measures can be collected and calculated based on stance time between the amputated and intact limb and used as an intervention to alter walking mechanics[14]. Using a simple pre- and post-test design, stance time symmetry has been shown to improve after six, 30-minute sessions of symmetry training over the course of three weeks. This symmetry training involved individuals with below knee amputation walking while wearing the LEAFS system and being monitored by a licensed physical therapist and an audible ‘beep’ when the individuals fall below a preset threshold for stance time symmetry. This indicates that there is ability to alter temporal measures in individuals with lower extremity amputation.

There is conflicting evidence regarding spatiotemporal symmetry in individuals with lower extremity amputation. Some studies indicate that some individuals with below knee amputation demonstrate symmetry in spatiotemporal measures like step length but continue to have increased variability of measures like covariance of residual limb variability and step length variability during self-selected walking when compared to healthy individuals[181]. This indicates although the step lengths may be similar, the individual with transtibial amputation has a ‘less stable’ gait pattern when compared to healthy controls in terms of step length. Results of stance symmetry reveal that only a subset of individuals with transtibial amputation spend more time on their sound limb, while other spend increased time on the amputated limb[73]. This information indicates that spatiotemporal asymmetries likely depend on factors other than simple diagnosis of amputation.

Given the underlying gait asymmetry in individuals with lower extremity amputation, and the ability to demonstrate meaningful change when prompted, we proposed an experiment to better understand the relationship of two key gait variables (peak trailing limb angle and anterior ground reaction force) symmetry with use of visual feedback. In our experiment we evaluated the impact of symmetry defined by anterior ground reaction forces on trailing limb angle and vice versa. Neither has been evaluated in the literature for individuals with lower extremity amputation.

Literature Review Summary

Individuals with lower extremity amputations exhibit a variety of alterations to their self-selected walking pattern. Why individuals select these altered gait patterns is unclear, although the selection may be influenced by safety, efficiency, and normal appearance of functional ability. It has been argued that returning to walking symmetry in a system that does not have the componentry required for symmetry is unrealistic; however, clinical treatment often focuses on maximizing symmetry, particularly of spatiotemporal measures. This clinical approach seems to ignore the underlying kinetic needs and impact of force generation on kinematic variables. Clinicians see that the forces are different between the intact and prosthetic limbs, yet we expect spatiotemporal symmetry and a return to normal walking pattern. Readily available and prescribed prosthetic componentry has not achieved enough force production at the foot to overcome the loss of the primary muscle group responsible for propulsion while simultaneously allowing for improved feedforward and feedback mechanisms for balance. This study will provide insight into the relationship between anterior ground reaction force and trailing limb angle in individuals with below knee amputation. This essential first step will be used to understand the potential relationship between propulsion and trailing limb angle but also to provide a foundation to explore the impact of visual feedback, amount of time required for adaptation, and potential for use of a kinematic variable like trailing limb angle to alter kinetic output in individuals with lower extremity amputation.

Chapter 3: Specific Aims and Methods

Introduction to Specific Aims and Methods

Individuals with unilateral below knee amputation (BKA) have difficulty generating a symmetric walking pattern that matches age matched healthy controls. This asymmetry may lead to chronic secondary conditions, resulting in reduced mobility and increased mortality. **In individuals with unilateral below knee amputation, the underlying kinematic and kinetic asymmetries observed during steady state walking and the relationships between these variables are not well understood**. Despite the lack of clear consensus and understanding surrounding the impact of these asymmetries, current clinical care attempts to reduce any observed kinematic, kinetic, and spatiotemporal asymmetries. During normal, healthy, steady-state walking, forward acceleration to overcome braking forces and move the center of mass forward requires the generation of anterior ground reaction forces (AGRF). The production of these anterior ground reaction forces is often called 'propulsion', a term we may occasionally use interchangeably throughout this document. Asymmetry of propulsion is often considered to be a result of altered contributions to anterior force generation by the foot and ankle of the amputated lower extremity[35,42,146,149,151,182]. Propulsion, which may be defined as peak anterior force or the positive integral of the anteroposterior force curve with respect to time (impulse), can be influenced by not only force production of the hip extensors and plantar flexors, but also potentially by the ipsilateral trailing limb angle (TLA). Our goal was to determine the effects of manipulating TLA on AGRF, and similarly determine the effects of manipulating AGRF on TLA using real time visual feedback while walking on an instrumented treadmill without upper extremity support. We believed that this investigation could provide information about a potential relationship between trailing limb angle—which is arguably easier to assess using available technology in the clinical setting—and a kinetic variable, anterior ground reaction force. We posited that this investigation could provide information to inform the clinical practice of and potential future study of training programs to reduce asymmetry in individuals with lower extremity amputation. This investigation also used visual feedback to explore the interrelation of kinetic and kinematic gait variables in individuals with lower extremity amputation. Furthermore, the results observed may hopefully encourage the investigation of innovative visual feedback paradigms and programs for short- and long-term alteration of gait asymmetries in individuals with lower extremity amputation.

Recent work among stroke survivors implicated trailing limb angle as a key component of propulsion,[36,37,41,160,183] as proper positioning of the trailing (posterior) limb during gait is critical to the generation of propulsion during terminal stance. In the absence of active musculature at the ankle and foot, it is theoretically possible that individuals with lower extremity amputations may be able to increase propulsion in a way like stroke survivors by increasing the trailing limb angle. Increasing trailing limb angle may result in a larger portion of the ground reaction force being anteriorly directed during push-off. The amount of push-off or propulsion generated by increasing trailing limb angle individuals with lower extremity amputation is unknown but could be a consequence of increased use of mechanical properties of the prosthesis, thereby maximizing output from a passive device. While true in recent literature investigating this concept in post stroke survivors, **it is unknown if individuals with unilateral lower extremity amputation can increase residual limb propulsion by increasing TLA.** The main goal of this research was to quantify the effect of trailing limb angle on anterior ground reaction force in individuals with unilateral below knee amputation and their otherwise healthy control counterparts. We proposed a single session data collection of individuals with below knee amputation and healthy control adults with and without a solid ankle foot orthosis to determine the relationship between trailing limb angle and anterior ground reaction force.

Recruitment and Participant Selection

We planned to recruit twenty-four (24) individuals with amputation from prosthetists, physicians, physical therapists, and associated medical clinics using established clinician relationships with study staff and word of mouth in the greater Charleston, South Carolina area. Additionally, thirteen (N=13) healthy control individuals were to be recruited by word of mouth in the Medical University of South Carolina and Charleston area for participation as otherwise healthy control adults. A master list was generated for communication and recruitment of individuals with below knee amputation in the Charleston and surrounding areas that included but was not limited to: 1) All O&P clinic locations representing the five major prosthetic providers in the area (Floyd Brace Company, Hanger Clinic, Carolina Orthotics and Prosthetics, Charleston Brace Company, and the Medical University of South Carolina O&P; 2) Two physicians that perform the majority of lower extremity amputations as determined by consulting the prosthetist about their primary referral sources (one orthopedic surgeon and one vascular surgeon); 3) all in-patient and sub-acute rehabilitation hospitals (MUSC Rehabilitation Hospital, formerly Encompass Health, formerly HealthSouth Rehabilitation Hospital, Roper Rehabilitation Hospital, and Vibra Hospital formerly Kindred Hospital); 4) three major local in-patient acute care hospital physical rehabilitation departments (Medical University of South Carolina, Ralph H. Johnson Veteran Affairs Medical Center, and Roper Hospital); 5) all amputee support groups listed within approximately a 100 mile radius from downtown Charleston, South Carolina; 6) all available online support and information groups for individuals with lower extremity amputation(s); 7) home health agencies serving patients in the Charleston/Dorchester/Berkley county area; and 8) all professional relationships of individuals that were currently treating in an area that might encounter an individual with a lower extremity amputation. All fliers and advertisements created were approved by the Medical University of South Carolina Institutional Review Board and were posted in public locations and local clinics with semi-routine follow up.

Any individuals who wished to participate were instructed to contact the study coordinator or PI to receive additional information. Healthcare providers (e.g., prosthetists, MDs, PTs) received information from study staff regarding the existence of this study but they were not allowed to consent potential participants. Any of their patients that expressed interested were instructed to contact the PI, coordinator, or approved study staff via telephone or email for potential screening. Participation in this study was independent of clinical care. Sample size calculation was completed *a priori* for the Aims and experiments for individuals with below knee amputation, separately from the Aims and experiments for the otherwise healthy control participants.

Prior to consent, interested individuals had all procedures, study rationale, time commitment, and any pertinent information explained to them over the phone without recording any data or protected health information. If the individual agreed to participate, they were scheduled for their consent and study visit with the appropriate study personnel. The consent process was completed according to IRB best practices for clinical research, and participants were granted the opportunity to have all questions answered. The consent process occurred in private or semi-private location to allow for privacy and confidentiality. A copy of the informed consent form and notice of privacy practices was made available to all enrolled participants. All consent and data collection documentation were approved by The Medical University of South Carolina Institutional Review Board. The level of amputation and healthy control status was determined by a licensed physical therapist in conjunction with patient report. Enrollment was not based on demographic factors including but not limited to race, ethnicity, sex, sexual identity, sexual orientation, or socioeconomic status. Students and employees of Medical University of South Carolina or the Ralph H. Johnson Veterans Affairs Medical Center were permitted to participate with no undue coercion or influence.

Individuals with Below Knee Amputation Participants:

Inclusion Criteria: 1) Unilateral lower extremity loss below the knee and above the ankle; 2) Ability to walk with prescribed lower extremity prosthesis without external assistive devices; 3) Ability to stand with or without assistance of external devices (canes/crutches/assistive devices); 4) Age 18-89; 5) Functional active range of motion of intact joints of both lower extremities sufficient for walking; 6) Full extension (0^o) passive range of motion of both knees; 7) Passive bilateral hip range of motion to a minimum of 5^o extension; 8) Ability to provide written informed consent.

Exclusion Criteria: 1) Any unstable cardiac or pulmonary condition that limits mobility; 2) Open or non-healed wounds on the residual limb; 3) Concomitant neurological disorder impacting mobility or balance (e.g. stroke, spinal cord injury, Parkinson's Disease, Multiple Sclerosis, Amyotrophic Lateral Sclerosis (ALS)); 4) Previous lower extremity fracture or joint replacement of the remaining joints; 5) Any unstable medical comorbidity or condition that limits their expected life to less than one year from the date of enrollment.

Healthy Control Participants:

Inclusion Criteria: 1) Age: 18-50, 2) Ability to provide informed consent, 3) Ability to safely walk without the use of external braces or device.

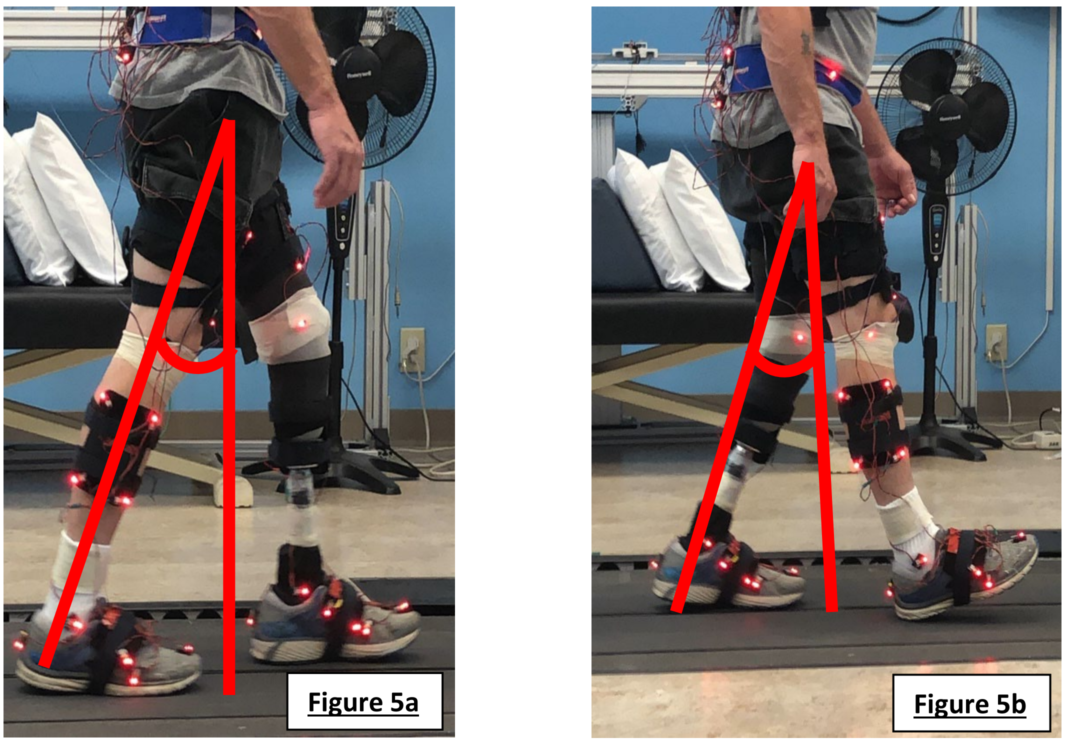
Exclusion Criteria: 1) Significant lower extremity injury requiring surgery (e.g., joint replacements, non-healed fractures, amputation, etc.); 2) Any systemic disorder that negatively impacts mobility and walking ability (e.g., cardiac, pulmonary, connective tissue, neurological etc.); 3) Significant vision dysfunction; 4) Life expectancy less than one year; 5) Weight greater than 350 lbs.

Equipment and Data Definitions

We collected, analyzed, and reported symmetry indices on the peak trailing limb angle and peak anterior ground reaction force that incorporates values from the intact and prosthetic limb of the individual with below knee amputation, or control and experimental limbs in the healthy control participants. With respect to propulsion the anterior ground reaction force symmetry index calculated from the peak forces was the primary outcome measure of interest and the symmetry index from impulse values was used as a secondary outcome measure.

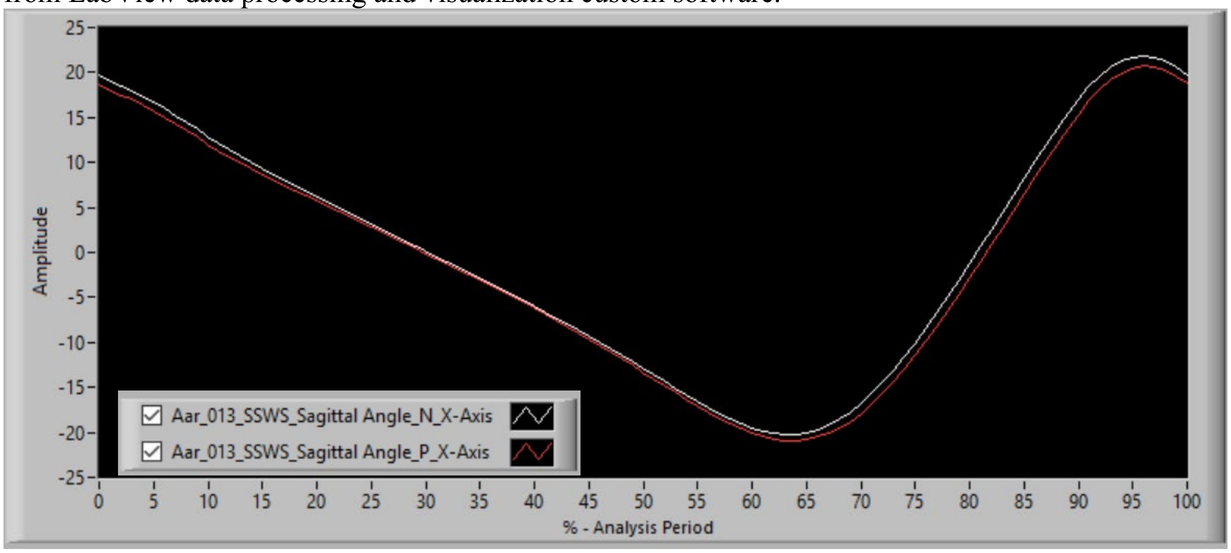
Trailing limb angle: The peak (maximum) sagittal plane angle was calculated from the pelvis center of mass to the reference foot center of mass in the laboratory reference frame. Similar definitions have been used in the past to describe trailing limb angle during walking[35,183,184]. Measurements are presented in degrees (angle) for each limb during walking (Figure 5).

Figure 5: Trailing limb angle: Trailing limb angle is measured and reported in degrees as the angle between the two vectors joined at the pelvis. Figure 5a is an example of intact trailing limb angle, and Figure 5b is the prosthetic trailing limb angle. These two measures will be used to calculate peak trailing limb angle symmetry index.



Equipment: An active motion capture system, PhaseSpace (©PhaseSpace 2017), was used to measure marker position during static (standing as still as possible without moving) and dynamic (walking) trials. A total of forty-four (44) individual LED lights were placed on the pelvis, bilateral thighs, shanks, and feet along with knees and ankles (Figure 4). For the prosthetic limb, ankle markers were placed on the approximate center of rotation of the prosthetic ankle/foot component, ideally near the height of the intact ankle. Knee markers were placed on the prosthesis of the amputated limb in alignment with the axis of rotation of the knee. Custom software written by engineers at the Medical University of South Carolina – Center for Rehabilitation Research in Neurological Conditions were used to collect, process, and export the data for analysis. Marker data were collected at 120 Hz, with example trailing limb angle values during a stride shown in Figure 6.

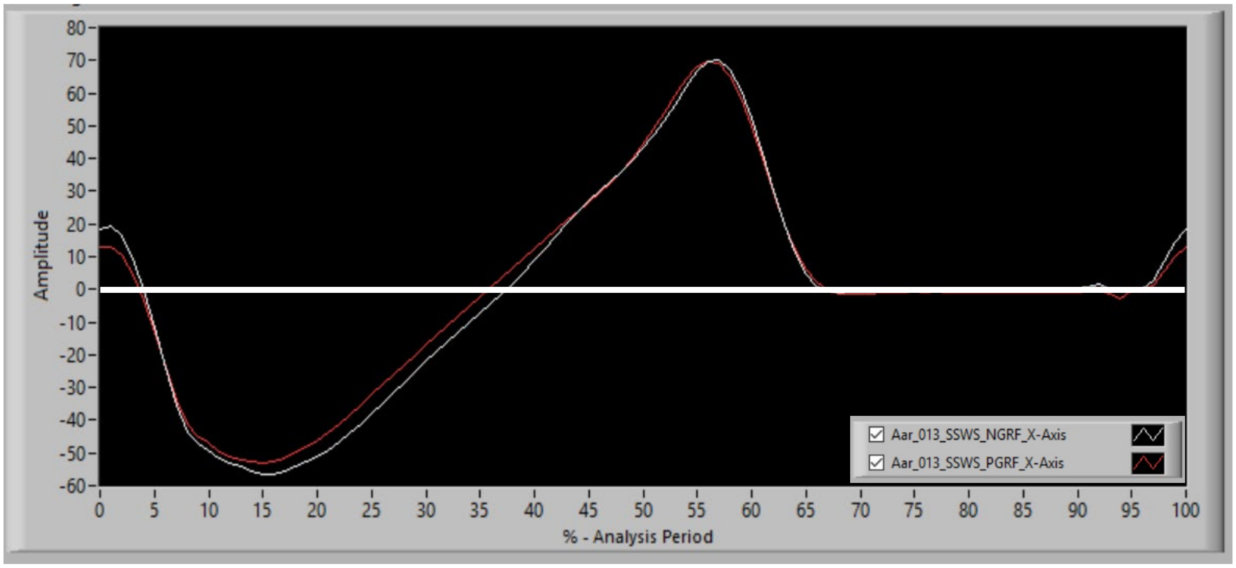
<u>Figure 6: Trailing Limb Angle Data Example:</u> Peak trailing limb angle representation output from LabView data processing and visualization custom software.



<u>Anterior Ground Reaction Force</u>: Peak (maximum) anterior ground reaction forces were measured under each foot as they were generated during the forward movement of the body's center of mass (COM) over the reference foot in stance (Figure 7). This is a common measure[6,185] and was reported in Newtons/kg (normalized by participant body mass).

<u>Equipment</u>: A Bertec (©Bertec Corporation) instrumented treadmill was used to collect three-dimensional ground reaction forces and moments at 120 Hz. In this investigation we focused exclusively on the anterior component of the anterior/posterior ground reaction force. The treadmill has two separate belts, one for each lower extremity that is synced to the PhaseSpace system through custom software written by engineers in the Center for Rehabilitation Research in Neurological Conditions at the Medical University of South Carolina.

<u>Figure 7: Anterior/Posterior Ground Reaction Force:</u> Example of the visual representation of anterior and posterior (sagittal plane) ground reaction forces for each limb average for a trial completing the gait cycle. Anterior ground reaction forces are found during the above zero portion (Zero = solid white line).



<u>Symmetry Values:</u> Symmetry values were calculated to generate a single value that quantifies potential interlimb differences (differences between the intact and prosthetic or control and encumbered limbs). A value of 0.5 indicates perfect symmetry between the intact and prosthetic (or control and encumbered) limb. A value that approaches zero (0.0) occurs when the prosthetic (encumbered) limb has a smaller value when compared to the intact (control) limb. A value closer to one (1.0) indicates a larger prosthetic (encumbered) limb value than intact.

Aims 1-3:

$$TLA\ Symmetry = Prosthetic\ TLA\ /\ (Prosthetic\ TLA + Intact\ TLA)$$

$$GRF\ Symmetry = Prosthetic\ GRF\ /(Prosthetic\ GRF + Intact\ GRF)$$

Aims 4 &5:

$$TLA\ Symmetry = Encumbered\ TLA\ /\ (Encumbered\ TLA + Control\ TLA)$$

$$GRF\ Symmetry = Encumbered\ GRF\ /(Encumbered\ GRF + Control\ GRF)$$

Data Collection

We planned to perform all procedures described below for each participant in one day if possible. A second day was permitted to complete all trials if the participant was unable to complete the trials in one day due to time or physiological restrictions. Two individuals with below knee amputation were scheduled to return for a second day due to elevated blood pressure readings after consent, demographic information, and clinical data collection. See Appendix A for the data collection sheet for Aims 1-3, and Appendix B for Aims 4 & 5.

Treadmill Walking Conditions

During all treadmill walking conditions, participants wore a harness attached to an overhead safety rail to prevent falling to the ground. Study staff were also present to ensure safety during walking, and the treadmill could be stopped if the participant became tired or needed to stop walking suddenly. Participants were instructed to walk using their natural walking pattern, but to be mindful of treadmill position with verbal reminders from study staff when necessary, to make sure each foot fall was on its appropriate treadmill belt for all trials (i.e., left foot on left treadmill belt, and right foot on right treadmill belt).

<u>Static</u>: Participant stands still on the treadmill with no assistance. This trial lasts five (5) seconds and provides a model of the participant's limbs for subsequent movement trials.

<u>SSWS</u>: Self-selected walking speed – The participant elects their walking speed and walks to determine their normal comfortable walking speed to be used in all subsequent trials.

<u>Baseline</u>: The same speed elected by the participant in the self-selected walking speed to gather data for both trailing limb angle and ground reaction forces.

<u>Matched TLA</u>: Real time visual feedback is provided to the participant to 'Match' the trailing limb angles for both legs from the Baseline trial.

Matched GRF: Real time visual feedback is provided to the participant to 'Match' the peak anterior ground reaction forces for both legs from the Baseline trial.

Symmetry TLA: Real time visual feedback is provided to the participant with instructions to generate as equal as possible peak trailing limb angle for the intact (control) and prosthetic (encumbered) limbs.

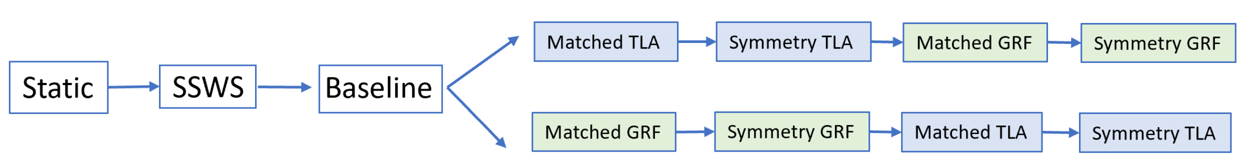
Symmetry GRF: Real time visual feedback is provided to the participant with instructions to generate as equal as possible peak anterior ground reaction force for the intact (control) and prosthetic (encumbered) limbs.

Asymmetry TLA: Real time visual feedback is provided to the participant with instructions to generate a 5% difference between peak trailing limb angle produced by the intact (control) and prosthetic (encumbered) limbs.

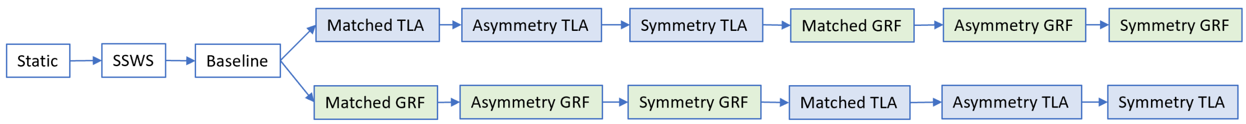
Asymmetry GRF: Real time visual feedback is provided to the participant with instructions to generate a 5% difference between anterior ground rection forces produced by the intact (control) and prosthetic (encumbered) limbs.

Treadmill walking trials were block randomized based on outcome measure (i.e., 1:1 random allocation of either the AGRF or TLA feedback program first with all trials associated with a given feedback type occurring in order) following the self-selected walking speed determination and Baseline trials. (Figures 8-10) (https//www.random.org/list/).

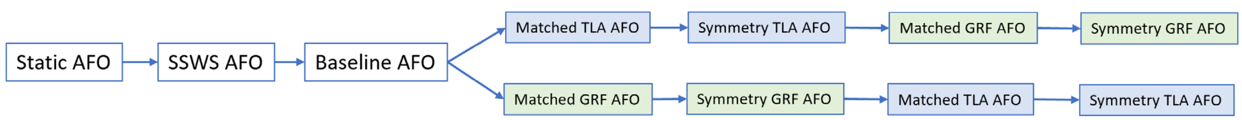
Figure 8: Treadmill Walking Conditions: Aim 1-3: Individuals with below knee amputation were block randomized to complete either the trailing limb angle real time visual feedback or peak anterior ground reaction force visual feedback first. Once completed, participants would complete the other trials.



<u>Figure 9: Treadmill Walking Conditions: Aim 4:</u> Healthy control participants were block randomized to complete all trials associated with either trailing limb angle or peak anterior ground reaction first. Once they completed all trials, the participants completed the trials associated with the remaining real time visual feedback.



<u>Figure 10: Treadmill Walking Conditions: Aim 5:</u> After completing all trials in Aim 4, healthy controls were fitted with a solid ankle foot orthosis and completed the trials in the same order as Aim 4.



The custom program used to provide visual feedback was written in LabView (©2019 National Instruments) by an engineer (Mrs. Heather Knight) at the Medical University of South Carolina. Visual feedback was provided using a subset of the total marker set (midpoint intersection of two inferior pelvis markers on the four-marker pelvis cluster and a single marker on the heel of each foot). For all treadmill walking trials (healthy control and individuals with lower extremity amputation), the walking speed was set as the individual's self-selected walking speed. Once the participant determined their own self-selected speed, this speed was maintained for all the trials within the experimental condition. During the experiments in Aims 4 & 5, participants were given separate opportunities to select their walking self-selected walking speed with and without the solid ankle foot orthosis. The self-selected walking speeds with and without solid ankle foot orthosis did not have to match and were intended to represent a normal/usual/comfortable walking speed within the constructs of their current state (i.e., with or without solid ankle foot orthosis). For data collections associated with experiments in Aims 1-3, all treadmill walking trials, except for the initial self-selected walking speed (SSWS) 30-second trial, were completed at the self-selected walking speed and lasted five (5) minutes. For Aims 4 & 5 investigating gait mechanics of healthy control participants, all treadmill walking trials were two (2) minutes in length, except for the self-selected walking speed (SSWS) 30-second trial.

Self-Selected walking speed determination and acclimation (SSWS)

Participants first walked on a treadmill without rails or upper extremity support to determine their self-selected walking speed. Precise instructions were provided to "determine your usual customary walking speed during normal daily functional activity". This speed was further described as "not slow, not fast, but your average walking speed that you walk during the day" and "a walking speed that you could walk and talk without getting too tired but get where you need to go without taking too long" if the initial cue was not understood. If the participant continued to struggle to self-determine their comfortable walking speed, a clinical subjective determination was made to identify the treadmill speed to be used. This determination was based on the participant's ability to remain in the center of the treadmill while walking safely (i.e. moving too far forward without becoming fatigued quickly generally indicates the ability to walk faster comfortably, whereas drifting towards the rear of the treadmill, balance difficulty, significantly altered walking pattern, or rapid induction of fatigue with shortness of breath indicate the speed is too fast and should be slowed to better approximate self-selected walking speed). During this period, no data were collected, and the participant was questioned to ensure they were walking at their 'normal' speed. The treadmill speed was increased to the participant's tolerance until they reported going faster than they felt was their normal speed. At this point the treadmill speed was reduced by 0.1 m/s and the treadmill came to a stop after a brief acclimation period. Adjustments up or down by 0.05 m/s were permitted during the acclimation period to identify as precisely as possible the participant's self-selected walking speed. One 30 second trial (SSWS) was collected to ensure equipment and software function and confirm the participant's self-selected walking speed. A brief preview prior to collecting data was performed to check that ground reaction force and marker data resemble the walking pattern observed.

Baseline walking trial (Baseline)

During this trial, participants walked at their previously determined self-selected walking speed. This trial was five (5) minutes for the individuals with lower extremity amputation and two (2) minutes for the healthy control participants. No visual feedback or verbal cues were provided during this trial but the screen that will later display feedback was present in front of the treadmill. Kinematic and kinetic data, including but not limited to trailing limb angle and anterior ground reaction force production respectively, were collected during this trial for implementation during the subsequent visual feedback trials and statistical analysis. This trial is what was used as the first data point in the paired t-test in the statistical analysis for Aims 1, 2, 4, & 5 for each corresponding outcome variable. The data collected during the Baseline trials also served to explore correlations between peak trailing limb angle and peak anterior ground reaction force in Aim 3 – Objective 1, and supplemental analyses associated with healthy control participants.

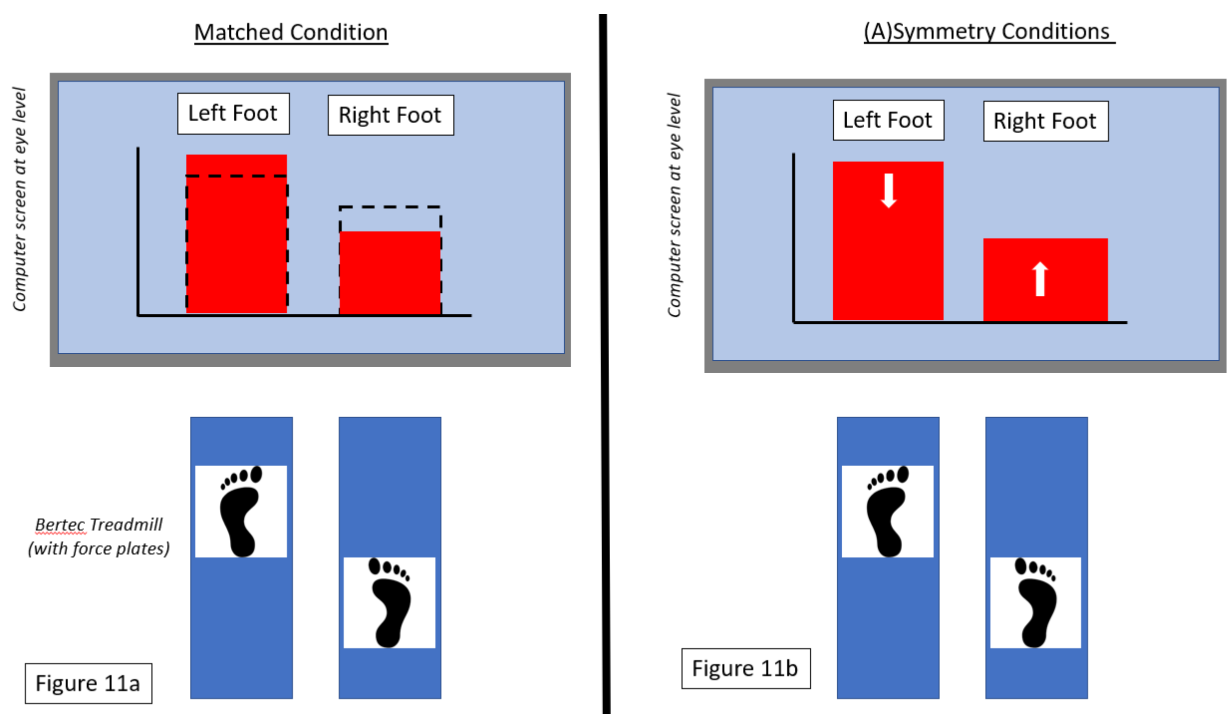
> Baseline: Trailing Limb Angle (TLA) and Peak Anterior Ground Reaction Force (GRF) generated by the participant during the Baseline trial.

Note: Trials labeled with "AFO" represent Aim 5 in which healthy control participants will wear a solid ankle foot orthosis (AFO).

Visual Feedback to Match Variable of Interest's Baseline Average (Matched-)

Once the SSWS and Baseline trials were completed, participants then received visual feedback related to either peak trailing limb angle or peak anterior ground reaction force production depending on their block randomization order. The visual feedback was provided using a monitor placed in front of the treadmill at the participant's eye level. The visual feedback representation for the 'Matched' trials had two primary elements: a static dashed outline and a solid bar area for each foot (Figure 10a). The empty dashed outlined pair of boxes remained unchanged for the duration of the trial and demonstrated the calculated average peak trailing limb angle or average peak anterior ground reaction force produced for each leg during the Baseline trial depending on the block randomization order. This pair of boxes (one for the left foot and one for the right) served as the targets for each leg during the 'Matched' real time visual feedback trial. The second element of the 'Matched' representation was a solid box that represented individual real time visual feedback variable (either peak trailing limb angle or peak anterior ground reaction force) observation for the immediately completed step.

Figure 11: Real Time Visual Feedback: Visual representation of the real time visual feedback provided to participants during treadmill walking. **Figure 11a: Matched Outcome Condition**: Representation of the visual feedback during the matched trial. During the matched trial subjects were asked to 'fill the dashed line box with the red bars' for each step and on each foot. They were informed that the red bars would change with each step, but the dashed box would remain. The dashed box was calculated from the average of all steps during the Baseline trial. **Figure 11b: Symmetry Outcome Condition:** Representation of visual feedback screen provided to participants with instructions about which outcome variable they are demonstrating to make the two red bars equal height.



Participants were instructed to match the mean Baseline average represented by the dashed box, with each step, represented by the solid red bar. Verbal instructions were provided tailored to the real time visual feedback variable. Instructions were consistent for key pieces of information and stated: "In front of you there is a screen with dashed boxes and solid bars. Can you see the dashed box and the solid bars?" The participant would answer in the affirmative, which allowed us to proceed. "Your goal during this trial is to fill in the dashed boxes with the solid bar. The dashed boxes will not change, but the red bar will move with every step. The solid bar represents what you are doing with each step. The left side of the screen is for your left foot. The right side of the screen is for your right foot. Your goal is to match each step on the left and right with the corresponding dashed box. Do you understand the instructions?" The participant would answer in the affirmative, which allowed us to proceed. "During this trial, the solid bar represents how far your foot is behind you at each step (*for the Matched peak trailing limb angle trial)* / how hard you are pushing off with each step (*for the Matched peak anterior ground reaction force trial)*. The further behind you your foot goes, the higher (larger) the bar will be on the screen (*for the Matched peak trailing limb angle trial) /* the harder you push off with each step, the higher (larger) the bar will be on the screen (*for the Matched peak anterior ground reaction force trial)*. Do you understand the instructions and the goal of this trial?" The participant would answer in the affirmative to begin the trial and data collection. No additional information was provided to give the participant any information about the outcome measure that was studied. Participants were not instructed of a "correct" method to change the outcome measure using the real time visual feedback variable. Kinematic (e.g., trailing limb angle) and kinetic (e.g., anterior ground reaction force) data were collected continuously for the duration of the walking trial. This trial was five (5) minutes for individuals with below knee amputation (Aims 1-3) and two (2) minutes for healthy control participants (Aims 4 & 5). Verbal reminders of the goal and desired action (i.e., fill in the dashed box with the solid bar, and the bar represents how far behind you, your foot is with each step (*trailing limb angle*) / how hard you are pushing off with each step (*anterior ground reaction force*)) were provided during the trial. Verbal encouragement of performance was not allowed or given during any of the trials. There will be four trials with this general nomenclature: Matched TLA, Matched GRF, Matched TLA AFO, and Matched GRF AFO.

> Matched TLA: In this trial, participants were presented with visual feedback and instructions to match the Trialing Limb Angle (TLA) presented for the right and left leg from the Baseline trial.
>
> Matched-GRF: In this trial, participants were presented with visual feedback and instructions to match the peak Anterior Ground Reaction Forces (GRF) presented for the right and left leg from the Baseline trial.

Note: Trials labeled with "AFO" represent Aim 5 in which healthy control participants will wear a solid ankle foot orthosis (AFO).

Visual Feedback to Prescribe Symmetry of the Variable of Interest (Symmetry-)

These 'Symmetry' trials were completed using real time visual feedback and supplemental verbal instructions aimed at encouraging the achievement of either peak trailing limb angle or peak anterior ground reaction force symmetry depending on the Aim and experiment. Participants were instructed to make the bars representing the left and right foot on the screen the same size during symmetry trials, while not focusing on the amplitude (height) of the bars themselves. Verbal instructions supplemented what was provided during the 'Matched' trial. A brief review of what was being displayed and orientation to the screen itself. Instructions were stated and updated to reflect the goal of the trial: "Now you should only see the solid bars on the screen. During this trial, your goal is to make those two bars the same height on the screen. It does not matter if they are towards the bottom, top, or middle as long as you do whatever you need to do to make the two bars the same height. Like the previous trial, the farther your foot is behind you, (*trailing limb angle) /* the harder you push off with each step (*anterior ground reaction force)*, the bigger that bar will be on the screen. Do you understand the instructions and the goal of this trial?" The participant would answer in the affirmative to begin the trial and data collection. This trial was five (5) minutes for individuals with below knee amputation (Aims 1-3) and two (2) minutes for healthy control participants (Aims 4 & 5). Verbal reminders of the goal and desired action (i.e., fill in the dashed box with the solid bar, and the bar represents how far behind you, your foot is with each step (*trailing limb angle*) / how hard you are pushing off with each step (*anterior ground reaction force*)) were provided during the trial. Verbal encouragement of performance was not allowed or given during any of the trials.

Symmetry TLA: During these trials participants were given real time visual feedback as well as verbal instructions to generate equal Trailing Limb Angles (TLA) for the left and right foot for the duration of the trial.

Symmetry-GRF: During these trials participants were given real time visual feedback as well as verbal instructions to generate equal peak Anterior Ground Reaction Forces (GRF) for the left and right foot for the duration of the trial.

Note: Trials labeled with "AFO" represent Aim 5 in which healthy control participants will wear a solid ankle foot orthosis (AFO).

Visual Feedback to Prescribe Asymmetry of the Variable of Interest (Asymmetry-)

In Aim 4, healthy control participants were asked to deviate from their Baseline symmetry and generate asymmetric output of either peak trailing limb angle or peak anterior ground reaction force. These trials were labeled 'Asymmetry' and were accomplished nearly identically to the 'Symmetry' trials. The unencumbered healthy control participants were asked to make the left and right boxes the same height. The instructions were the same as given in the 'Symmetry' condition, but the feedback program was intended to alter the real time visual feedback variable of interest's (i.e., peak trailing limb angle or peak anterior ground reaction force) symmetry index by 5% by requiring increased output from the experimental limb. Unfortunately, the program was inadvertently written and tested to only change the experimental limb output by 5%, not alter the symmetry index by 5%. What the participant saw on the screen was 95% of their actual production of the real time visual feedback variable of interest on the experimental leg. For example, if the healthy control participant generated 10 degrees of trailing limb angle on the experimental limb, the screen would reflect 9.5 degrees. The healthy control participant would then need to generate more of the outcome measure of interest (peak trailing limb angle or peak anterior ground reaction force) to match the control limb and generate symmetry. Thus, the participants did not actually knowingly and volitionally alter their output to a stated goal, but rather were instructed to generate symmetry, while the real time visual feedback provided asymmetric feedback.

Asymmetry TLA: During these trials participants were given real time visual feedback as well as verbal instructions to generate equal Trailing Limb Angles (TLA) for the left and right foot for the duration of the trial. During these trials, the individuals were largely unaware that they were in-fact being asked to generate asymmetric production of peak trailing limb angle between the two legs.

Asymmetry GRF: During these trials participants were given real time visual feedback as well as verbal instructions to generate equal peak Anterior Ground Reaction Forces (GRF) for the left and right foot for the duration of the trial. During these trials, the individuals were largely unaware that they were in-fact being asked to generate asymmetric production of peak anterior ground reaction forces between the two legs.

Note: Trials labeled with "AFO" represent Aim 5 in which healthy control participants will wear a solid ankle foot orthosis (AFO).

Fitting and use of Solid Ankle Foot Orthosis (Aim 5)

Healthy control participants enrolled in the study were first fitted with a solid ankle foot orthosis (SAFO) prior to completing Aim 4 or 5. A box of fabricated solid ankle foot orthoses donated by Floyd Brace Company were offered as potential options. Participants tried on SAFOs until one fit comfortably without significant discomfort or pain. All SAFOs had at 90 degree or neutral ankle according to the prosthetists and verified as measured by a goniometer. After the first five participants completed the study, there were two complete sets of solid ankle foot orthoses that were a general best fit. Subsequent participants were assigned in alternating fashion to either wear the left or right SAFO a priori to ensue near equal group size. If a participant found their assigned encumbered limb SAFO was uncomfortable they were offered the opportunity to try the other leg. Ultimately, all participants were able to select and fit into a SAFO without pain.

Figure 12: Solid Ankle Foot orthoses: Participants were fit with either the left or right solid ankle foot orthosis for Aim 5. Displayed here are one of two sets of custom neutral (90 degrees) solid ankle foot orthoses as measured by a goniometer were primarily used for all participants.

Once the limb that would be fit with the SAFO was determined, this limb would also serve as the experimental limb in Aim 4 and the encumbered limb in Aim 5. When Aim 4 was completed, all participants then donned the previously selected SAFO and were then fit with a laboratory issue shoe to go over the SAFO. This shoe was typically two to three sizes larger than their normal shoe size. The shoe was selected based on snug but comfortable fit. The participant wore their own shoe on the control limb. The SAFO was secured to the limb at two primary locations: superior shank around the gastrocnemius and ankle joint. All SAFOs had a hook and loop (Velcro) strap to secure the AFO to the shank, and some had a strap that secured the ankle into the heel cup. Additional latex free co-flex bandages were used in both locations to further secure the SAFO to the participant. Participants were questioned to make sure they were as comfortable as possible, but not in any pain or having any altered sensation or potential symptoms of vascular or nerve compromise due to excessive compression. Alterations were made, as necessary. Participants were then allowed to acclimate to the feeling of standing and walking in the SAFO before getting on the treadmill and questioned again for comfort and fit. Participants then completed all study procedures as prescribed (Figure 10).

Clinical Tests for Individuals with Below Knee Amputation (Aims 1-3)

The **Amputee Mobility Predictor** is a validated and commonly used clinical scale to assess the mobility function of individuals with lower extremity amputation[186]. There are two versions of the test: The Amputee Mobility Predictor (AMPnoPro) is completed without lower extremity prosthesis, and the Amputee Mobility Predictor with Prosthesis (AMPPro) which is completed with the lower extremity prosthesis. Since our study requires ambulation with a fitted prosthesis, the AMPPro was completed on individuals with below knee amputation that were enrolled in this study (Appendix C). This clinical scale provided an indication of study participants' functional mobility with the use of their prescribed prosthesis. The AMPPro has corresponding K-levels (K0 - K4) depending on their sum score. Individuals classified as K4 have the ability or potential for prosthetic ambulation that exceeds basic ambulation skills, exhibiting high impact, stress, or energy levels. These individuals are commonly seen as active adults, athletes, or mobile children[186,187]. Individuals classified as K3 functional ambulators have potential for variable cadence, able to traverse most environmental barriers in the community, and may have vocational, therapeutic, or exercise activity that demands prosthetic use beyond simple locomotion[186,187]. The K-level classifications also make it clear that lower-level ambulation profiles are reserved for individuals that cannot successfully ambulate without assistance or assistive device. Individuals that are K0 typically do not walk and only use their prosthesis for transfers, and K1 represents household ambulators that can only walk at a fixed cadence.

The **Houghton Scale** is a measure designed to quickly quantify functional outcomes of individuals with lower extremity amputation[188]. It has been shown to correlate with the K-level classifications found in Medicare regulations and integrated into the Amputee Predictor Mobility Scale[189]. Individuals with below knee amputation that were enrolled in this investigation completed the Houghton Scale (Appendix D) to provide additional insight about their wearing time and daily mobility with the lower extremity prosthesis.

Overground walking assessment: Overground walking data were collected using the GAITRite® walkway from CIR Systems, Inc on individuals with below knee amputation and healthy control subjects with and without solid ankle foot orthosis. Three trials of self-selected walking speed without walking aid or assistance were collected to review spatiotemporal measures as well as overground gait speed.

Demographic Information collection

Demographic information was collected to describe the participants as well as look for any trends related to demographics in future post hoc analyses (Appendix E and Appendix F). The factors of interest are age, gender, time since amputation, cause of amputation, prosthesis type, and limb involved, and were collected and stored on a single data collection form for each participant. Raw data collection forms for the Houghton Scale and AMPPro were stored separately in the participant's participation file.

Amputated limb length was measured as the distance from the anterior bisection of the medial and lateral knee joint line to the distal end of the lower extremity. Intact limb length was measured from the lateral joint line of the knee to the apex of the lateral malleolus. This measure may be used understand any differences in gait outcomes based on residual limb length. In our calculations, we used relative limb length as opposed to a raw length value to classify individuals with lower extremity amputation as having either short or long residual limb. For example, a tibia that is greater than or equal to 50% of intact limb is considered 'long residual limb', whereas less than 50% is considered a 'short residual limb'. The study was not powered to uncover any differences of responder versus non-responder based on limb length classification, but it may be used for exploratory analyses in the future.

Data Analysis Procedures

Due to the naturally occurring rhythmic bipedal gait cycle, the peak anterior ground reaction force and peak trailing limb angle occur only once during each gait cycle. Anterior ground reaction force (AGRF) is defined the above zero portions of the anterior/posterior ground reaction curve. For our analysis we extracted the peak (maximum) value and the positive area under the curve (Impulse) of the anterior ground reaction force curve. The anterior ground reaction force value for each step was evaluated between contralateral toe off and ipsilateral mid-stance.

Peak trailing limb angle is defined as the peak sagittal plane angle is calculated from the pelvis center of mass (COM) to the reference foot center of mass (COM) in the laboratory reference frame. Measurement is presented in degrees (angle) for each limb and is the minimum peak in the output. To determine the peak trailing limb angle, the entirety of the gait cycle was evaluated.

For both outcome measures, they symmetry index was then calculated and analyzed according to the a priori analysis plan. A custom LabView (© National Instruments) program calculated gait events and exported values collected from the lower body marker set (© PhaseSpace) and instrumented treadmill (© Bertec). Data were reviewed for quality and any incomplete steps or crossover events were deleted from analysis. Crossover events are when a participant inadvertently places the right foot on the left force plate or vice-versa while walking on the treadmill. This can be observed during either the single or double limb support phase of gait during a quality assurance assessment after data are collected and processed.

Although we collected data for the full five minutes, the data analysis only includes the final minute of the five-minute trials for individuals with below knee amputation. This should have allowed for sufficient time to understand, acclimate, and appropriately perform the prescribed walking pattern[54], while attempting to prevent fatigue across conditions[190]. For healthy control participants completing Aims 4 & 5, the data collected during the entire 2-minute trial were averaged to calculate the outcome variable symmetry index. In addition to the primary outcome measures, numerous other kinetic and kinematic gait measures are available for future exploratory analyses. Data were then exported into Microsoft Excel for organization into formats suitable for statistical analysis using SAS software Version 9.4 of the SAS System for Windows. SAS Institute Inc., Cary, NC, USA. An *a priori* Type-I error was set at 0.05 for all hypothesis tests in Aims 1, 2, 4, & 5.

Data Collection Contingency Plans

1) In the event a study participant with below knee amputation was unable to walk continuously for prescribed five-minute trial, they were permitted a rest break and the trial was to be re-initiated if they did not complete at least two (2) minutes of walking. Prior to stopping the trial, participants were encouraged to complete the trial safely if possible was provided. If the participant completed a minimum of two (2) minutes, the data were used for the final minute completed and analyzed according to the a-priori plan. This change in the protocol was noted in the participant's record and reported appropriately. This occurred with only one participant during the Baseline trial, but he was able to complete all other trials at the prescribed duration.

2) If an individual was unable to complete all trials in a single visit due to time restrictions or limitations, a second testing day was allowed within seven (7) calendar days if there had been no significant medical or functional alteration or prosthetic change. Data collection was attempted at the same time of day to mitigate the effect of time-of-day performance and limb size daily fluctuations. Baseline data were only collected once and were used for the values on the second day. Two individuals required a second day due to elevated blood pressure readings before treadmill walking assessments. These two individuals were able to complete the consent, overground walking assessment, and clinical assessments. The second day of testing was scheduled but not completed due to COVID-19 facility closures. These two individual's data are not used in the hypothesis testing associated with Aims 1-3.

Specific Aims Analysis

Due to failure to recruit and test the planned sample size of individuals with below knee amputation, effect size calculations were reported for Aims 1 and 2. These data will allow for future sample size calculations and inform investigators about the impact of real time visual feedback on individuals with below knee amputation.

Aim 1: Quantify the effect of trailing limb angle visual feedback on gait symmetry measures in ambulatory individuals with below knee amputation.

Hypothesis 1: Visual feedback prescribing trailing limb angle symmetry will improve trailing limb angle symmetry.

Data collected from the Baseline and Symmetry TLA trials were used to analyze the effect of trailing limb angle visual feedback on the generation of trailing limb angle symmetry in individuals with below knee amputation. Average trailing limb angle symmetry during the Baseline trial was compared to Symmetry TLA. A paired two-tailed t-test was performed to determine if there was a difference in the symmetry with the implementation of a prescribed feedback. A significant result would have indicated that the prescribed visual feedback did alter trailing limb angle symmetry, i.e., the group symmetry index during the Baseline trial is different than the group symmetry index during the real time visual feedback trial to improve trailing limb angle. By looking at the direction of the change, we were able to identify if the symmetry improved or got worse with the implementation of the real time visual feedback.

> Planned statistical analysis: Paired two-tailed t-test alpha=0.05 comparing Trailing Limb Angle (TLA) symmetry index during the Baseline trial versus the Trailing Limb Angle (TLA) symmetry index in the Symmetry TLA trial.

Hypothesis 2: Visual feedback prescribing trailing limb angle symmetry will improve anterior ground reaction force symmetry.

Peak anterior ground reaction force symmetry during the Baseline trial was compared to peak anterior ground reaction force symmetry during the trial prescribing peak trailing limb angle symmetry using a paired two-tailed t-test. A significant result would have indicated that the anterior ground reaction force symmetry differs from the Baseline value with the implementation of the prescribed feedback for trailing limb angle symmetry. By reviewing the direction of the relationship, we posit the direction of the change in symmetry.

> Planned statistical analysis: Paired two tailed t-test $\alpha = 0.05$ comparing peak Anterior Ground Reaction Force Symmetry Index during the Baseline trial versus peak Anterior Ground Reaction Force Symmetry Index during the Symmetry TLA trial.

Aim 2: Quantify the effect of anterior ground reaction force visual feedback on gait symmetry measures in ambulatory individuals with below knee amputation.

Hypothesis 1: Visual feedback prescribing anterior ground reaction force symmetry will improve anterior ground reaction force symmetry.

Peak anterior ground reaction force data collected from the Baseline and anterior ground reaction force symmetry real time visual feedback trials were used to analyze the effect of peak anterior ground reaction force visual feedback on the generation of peak anterior ground reaction force symmetry in individuals with below knee amputation. A paired two-tailed t-test was performed to determine if there was a difference in the anterior ground reaction force symmetry with the implementation of prescribed feedback for anterior ground reaction force symmetry. A significant result would have indicated that the prescribed visual feedback did alter peak anterior ground reaction force production symmetry. By looking at the direction of the change, we posit that we were able to identify if the symmetry had improved or has gotten worse with the implementation of the prescribed visual feedback.

Planned statistical analysis: Paired two-tailed t-test $\alpha = 0.05$ comparing peak Anterior Ground Reaction Force Symmetry Index during the Baseline trial against peak Anterior Ground Reaction Force Symmetry Index during the Symmetry-GRF trial.

Hypothesis 2: Visual feedback prescribing anterior ground reaction force symmetry will improve trailing limb angle symmetry.

We compared the trailing limb angle symmetry during the Baseline and walking trial with prescribed peak anterior ground reaction force symmetry trials using a paired two-tailed t-test. A significant result would have indicated a difference in the trailing limb angle symmetry when a target for anterior ground reaction force symmetry is prescribed compared to the Baseline value. A subsequent review occurred to determine the direction of the change (i.e., more or less symmetrical).

Planned statistical analysis: Paired two tailed t-test $\alpha = 0.05$ comparing Trailing Limb Angle Symmetry Index during the Baseline trial versus Trailing Limb Angle Symmetry Index during the Symmetry-GRF trial.

Aim 3: Investigate the relationship between anterior ground reaction force symmetry and trailing limb angle symmetry in individuals with below knee amputation.

This aim was exploratory and sought to quantify a potential relationship between trailing limb angle and anterior ground reaction force production in individuals with below knee amputation. For these analyses, a series of correlations were performed. These following objectives allowed us to determine if there was a relationship between the two outcome variables at baseline, with the implementation of visual feedback for trailing limb angle symmetry, and with the implementation of real time visual feedback for peak trailing limb angle symmetry. While no direct statistical comparisons were planned across objectives in this Aim, the results could provide insight into the implications of the selection of visual feedback in altering the relationship between the two measures of symmetry.

Objective 1: Quantify the relationship between anterior ground reaction force symmetry and trailing limb angle symmetry when participants walk without visual feedback.

Statistical Test: Pearson correlation of Trailing Limb Angle Symmetry Index versus the peak Anterior Ground Reaction Force Symmetry Index during the Baseline trial.

Objective 2: Quantify the relationship between anterior ground reaction force symmetry and trailing limb symmetry when prescribing trailing limb angle symmetry.

Statistical Test: Pearson correlation of Trailing Limb Angle Symmetry Index versus the peak Anterior Ground Reaction Force Symmetry Index during the Symmetry TLA trial.

Objective 3: Quantify the relationship between anterior ground reaction force symmetry and trailing limb symmetry when prescribing anterior ground reaction force symmetry.

Statistical Test: Pearson correlation of Trailing Limb Angle Symmetry Index versus peak Anterior Ground Reaction Force Symmetry Index during the Symmetry GRF trial.

Aim 4: Quantify the effect of visual feedback on gait symmetry measures in healthy control individuals.

Hypothesis 1: Visual feedback prescribing anterior ground reaction force asymmetry will increase anterior ground reaction force asymmetry in the unencumbered healthy adult.

In Aim 4, healthy control participants were instructed to increase their asymmetry in the two outcome measures. For Aim 4, hypothesis 1, we sought to prescribe a 5% increase in peak anterior ground reaction force with the experimental limb. This 5% increase was based on a calculated average of peak anterior ground reaction forces generated in the experimental limb during the baseline trial. A significant result between the asymmetry cue and the baseline condition would have indicated that healthy control subjects demonstrated a difference in anterior ground reaction force symmetry index with the provision of real time visual feedback to alter symmetry by 5%.

Planned statistical analysis: Paired two-tailed t-test $\alpha = 0.05$ comparing peak Anterior Ground Reaction Force Symmetry Index during the Baseline trial versus the peak Anterior Ground Reaction Force Symmetry Index during the Asymmetry GRF trial.

Hypothesis 2: Visual feedback prescribing peak trailing limb angle asymmetry will increase peak trailing limb angle asymmetry in the unencumbered healthy adult.

Aim 4, hypothesis 2 followed the same plan and analysis as Aim 4, hypothesis 1 with the use of peak trailing limb angle as the outcome measure during the matched and asymmetry trials for trailing limb angle. A positive finding would indicate that there is increased asymmetry of trailing limb angle using visual feedback. A difference between the baseline and asymmetry trials indicated that healthy control individuals could alter their trailing limb angle with real time visual feedback.

<u>Planned statistical analysis</u>: Paired two-tailed t-test $\alpha = 0.05$ comparing Trailing Limb Angle Symmetry Index during the Baseline trial versus the Trailing Limb Angle Symmetry Index during the Asymmetry TLA trial.

Aim 5: Quantify the effect of visual feedback on gait symmetry measures in healthy control individuals wearing a solid ankle foot orthosis.

Hypothesis 1: Visual feedback prescribing anterior ground reaction force symmetry will improve anterior ground reaction force symmetry in the healthy adult wearing a solid ankle foot orthosis.

In Aim 5, hypotheses 1 & 2, the participants wore a solid ankle foot orthosis on only one leg which encumbers the ankle and thus would likely inhibit the ability to generate symmetric gait mechanics. In Aim 5, hypothesis 1, the focus was on the ability for subjects to use visual feedback to overcome this anterior ground reaction force asymmetry using visual feedback. This analysis mimicked Aim 1, hypothesis 1 with the goal of understanding if the asymmetry can be corrected in an analogous healthy control population. A positive finding here would have indicated that encumbered otherwise healthy control participants had a different peak anterior ground reaction force symmetry index using visual feedback when compared to the Baseline trial.

<u>Planned statistical analysis</u>: Paired two-tailed t-test $\alpha = 0.05$ comparing peak Anterior Ground Reaction Force Symmetry Index during the Baseline trial versus the peak Anterior Ground Reaction Force Symmetry Index during the Symmetry-GRF trial. Both trials were with healthy controls wearing an AFO.

Hypothesis 2: Visual feedback prescribing peak trailing limb angle symmetry will improve peak trailing limb angle symmetry in the healthy adult wearing a solid ankle foot orthosis.

Aim 5, hypothesis 2 followed the same plan and analysis as Aim 5, hypothesis 1 with the use of peak trailing limb angle as the outcome measure during the Baseline and asymmetry trials for trailing limb angle. A positive finding would have indicated that there was a difference in peak trailing limb angle symmetry when using visual feedback by healthy control individuals wearing a solid ankle foot orthosis when compared to the same subjects during the Baseline trial with AFO.

Planned statistical analysis: Paired two-tailed t-test $\alpha = 0.05$ comparing Trailing Limb Angle Symmetry Index during the Baseline trial versus Trailing Limb Angle Symmetry Index in the Symmetry TLA trial. Both trials were completed with healthy control participants wearing an AFO.

Sample Size Calculation

Aims 1-3: G*Power (©G*Power version 3.1.9.4) was used to determine the number of individuals required to complete the study. To detect a medium effect size of 0.6 with 80% power and an alpha of 0.05 using a paired sample t-test analysis, a total sample of 24 individuals is required. We are assuming a medium effect size because there are no current published effect sizes for real time visual feedback in individuals with lower extremity amputation (below or above knee). There are a variety of symmetry measure changes but none that investigate what we propose in this study, and none have published their effect sizes. Note: As a result of not meeting our recruitment goals, we reported effect sizes for Aims 1 and 2.

Aim 4 & 5:

G*Power (©G*Power version 3.1.9.4) was used to determine the number of individuals required to complete Aims 4 & 5. To detect a large effect size of 1.0, with 80% power and alpha of 0.025 (correction for multiple comparisons) using a paired t-test analysis, a total sample of 13 participants are required.

Feasibility testing

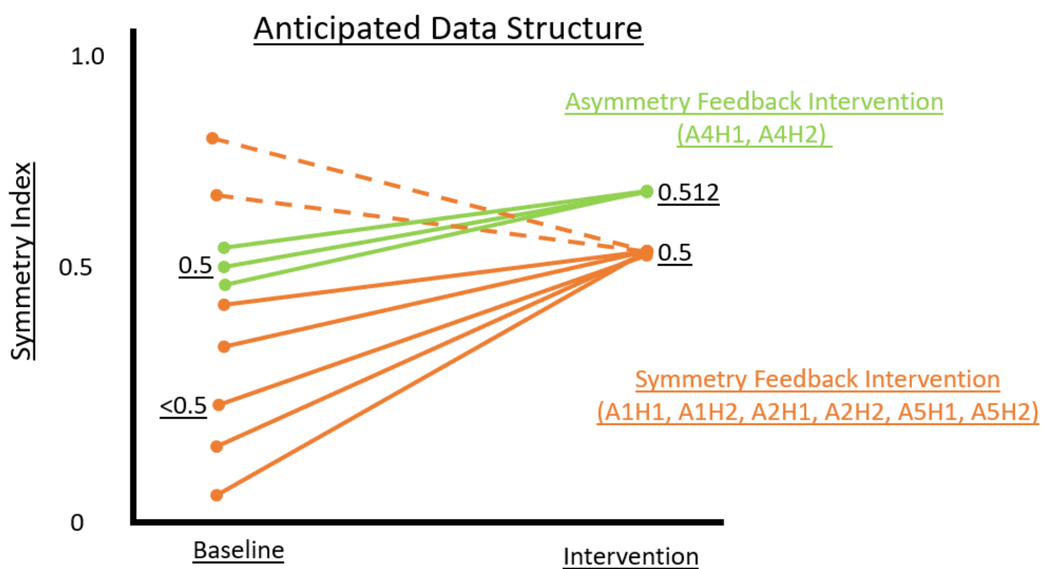
Prior to initiation of testing of individuals with lower extremity amputation population, a cohort of healthy controls completed the full and various portions of the final protocol. Since studies like this have not been completed, we tested healthy controls and provided feedback to either improve or worsen symmetry of both metrics. Healthy controls should present as largely symmetrical in their production of trailing limb angle and anterior ground reaction force production when walking at their self-selected walking speed. In this preliminary data collection feedback was provided to increase asymmetry of the outcome variable during the 'Matched' trial. If an individual demonstrated an asymmetrical walking pattern in either or both measures, we performed the protocol as described above to provide feedback to improve symmetry. We also completed a few trials to worsen symmetry measures in this population for a comprehensive review of improving and worsening symmetry in healthy controls using this protocol. These results are not presented here but were instrumental in establishing the protocol for Aims 4 and 5 and briefly assessing underlying assumptions about symmetry production in otherwise healthy control potential participants.

Anticipated Data Structure

Based on sound reasoning and collected background information we anticipated that the data would take a somewhat predictable form (Figure 13). For all Aims and Hypotheses that utilized real time visual feedback to improve outcome measure (peak trailing limb angle or peak anterior ground reaction force) symmetry, the data points with feedback should approach the symmetry index of 0.5. It was reasonable to believe that many of the individuals with lower extremity amputation (Aims 1 & 2) and healthy control participants wearing a solid ankle foot orthosis (Aim 5) would have started with asymmetry index less than 0.5 indicating a reduced value from the prosthetic or encumbered limb compared to the intact limb (solid orange lines). However, it was possible that some individuals may demonstrate the opposite with increased use of the prosthetic or encumbered limb during the baseline trial of the data collection (dashed orange lines). In Aim 4, we aimed to demonstrate increased asymmetry (decreased symmetry) via an increased use of the 'experimental' limb by 5%. Successful demonstration of this Aim could have yielded a data structure with a

Baseline symmetry index near 0.5 and Asymmetry value of 0.5 +5% or 0.512 (solid green lines). However, the real time visual feedback to increase asymmetry (worsen symmetry) in the unencumbered healthy control only altered the experimental limb 5%, which translates to an approximate symmetry index change between 1-2% from Baseline.

Figure 13: Anticipated Data Structure: For Aims 1, 2, and 5, we will utilize real time visual feedback to encourage symmetry in individuals with below knee amputation and healthy controls with solid ankle foot orthosis. Both groups are believed to be asymmetry in their generation of symmetric peak anterior ground reaction force and peak trailing limb angle, and by providing real time visual feedback, we should see an improvement. In Aim 4, unencumbered healthy control subjects should be symmetric at Baseline (0.5) and demonstrate an increase of 5% asymmetry using prescribed real time visual feedback.



Chapter 4: Results

Aims 1-3: Individuals with Below Knee Amputation

Eleven of the planned twenty-four participants with below knee amputation were enrolled, with only nine of those eleven completing all study procedures. Two of the eleven enrolled participants were unable to complete the treadmill walking assessment due to elevated resting blood pressure. Both were scheduled for follow-up visits that were subsequently cancelled due to the COVID-19 pandemic and facility closures.

The enrolled individuals demonstrated demographic heterogeneity reasonably representative of the geographical and clinical population studied (Table 1). Enrolled individuals with below knee amputation were predominantly white, non-Hispanic, and male. There was a heterogeneous etiology and near equal representation of limb involvement (Left=6 and Right=5). Participants had an average age of 57 years (SD=12) and limb loss chronicity of 89 months (SD=88) indicating a middle age average for limb loss and sufficient time to become accustomed to life with a prosthetic limb.

A variety of prosthetic feet were worn by participants and all except one were classified as *Energy Store and Release* (ESR). Participants' self-selected treadmill walking speed averaged just under 0.6 m/s and overground self-selected walking speed nearly 1.0 m/s, values that are well below normative values for age and gender matched healthy individuals[191]. Healthy age and gender matched normative average overground gait speed is approximately 1.35m/s[191]. The participants demonstrated AMPPro scores indicative of K2-K4 mobility classification. Most were classified as either K3 or K4 indicating that, at a minimum, they were able to successfully ambulate short distances without assistive devices. The Houghton scale yielded an average of just under 11 (range 9-12) indicating that participants are likely independent community ambulators[188].

Table 1: Demographic Participant Data for Aims 1-3: Participants in Aims 1-3 were individuals with below knee amputation. This table outlies their characteristics and clinical testing results.
*Subjects were randomized to complete testing using real time visual feedback of peak anterior ground reaction force or peak trailing limb angle. All participants completed feedback for both conditions.

Demographic Information (*n=11*)	**Number/ Mean**	**%/Std. Dev.**
Gender		
Male	8	73
Female	3	27
Race		
Caucasian/White	9	82
Native Hawaiian/ Pacific Islander	1	9
Black/African American	1	9
Ethnicity		
Hispanic/Latino	0	0
Non-Hispanic/Latino	11	100
Age (years)	57	12
Height (cm)	175	8
Mass (kg)	85	20
Overground Walking Speed (m/s)	0.99	0.16
Treadmill Walking Speed (m/s)	0.59	0.19
Functional Clinical Assessments *(n=11)*	**Mean (SD)**	**Range**
Houghton (0-12)	11 (1)	9-12
AmpPro (0-47)	42 (4)	35-47
Study Randomization* *(n=11)*	**Number/ Mean**	**%/Std. Dev.**
Anterior Ground Reaction Force (AGRF)	6	55
Peak Trailing Limb Angle (TLA)	5	45

Table 1a: Clinical description of individuals with below knee amputation.

Amputation Information (n=11)	**Number/ Mean**	**%/Std. Dev.**
Amputated Limb		
Right	5	45
Left	6	55
Etiology		
Elective	2	18
Non-Traumatic (Vascular)	4	36
Traumatic	4	36
Other	1	9
K Level		
K2	1	9
K3	5	45

K4	5	45
Chronicity (months)	89	88
Amputated Shank Residual Length (cm)	16	2
Intact Limb Length (cm)	39	3
Amputated Limb Range of Motion (degrees) *(n=11)*	**Mean (SD)**	
	Active ROM	**Passive ROM**
Hip		
Flexion	116(13)	123 (13)
Extension	9(8)	18 (8)
Knee		
Flexion	115 (21)	118 (20)
Extension	-2 (8)	4 (5)

Table 1b: Prosthesis information for individuals with below knee amputation: Prosthesis information for individuals with below knee amputation

Prothesis Information (n=11)	Number	%
Suspension Type		
Elevated Vacuum	1	9
Pin	6	55
Suction	2	18
Suspension Suction Sleeve	2	18
Pylon		
Standard	10	91
Standard with Soft Exoskeleton sleeve	1	9
Foot Type		
Ability Dynamics Rush 87	1	9
College Park - K2	1	9
College Park - Soleus	1	9
Freedom Innovation Kinterra Hydraulic	1	9
Freedom Innovation Maverick AT	1	9
Freedom Innovation Senator	1	9
Freedom Innovation Dynadapt Cat. 5	1	9
Odyssey	1	9
Proflex Pivot - Ossur	1	9
Rush 82 Ability Dynamics	1	9
Standard SACH	1	9
Prosthetic Provider		
Carolina Orthotics and Prosthetics	2	18
Floyd Brace Company	8	73
Medical University of South Carolina	1	9
Sock Ply during testing	4	Range 0-18

In Aims 1-3 a paired t-test was calculated and reported with all participants that were able to complete all the necessary walking trials. Effect size using Cohen's d. ($mean_1$-$mean_2$/SD) was also calculated in our results to demonstrate the impact of real time visual feedback on the outcome measures in each experiment.

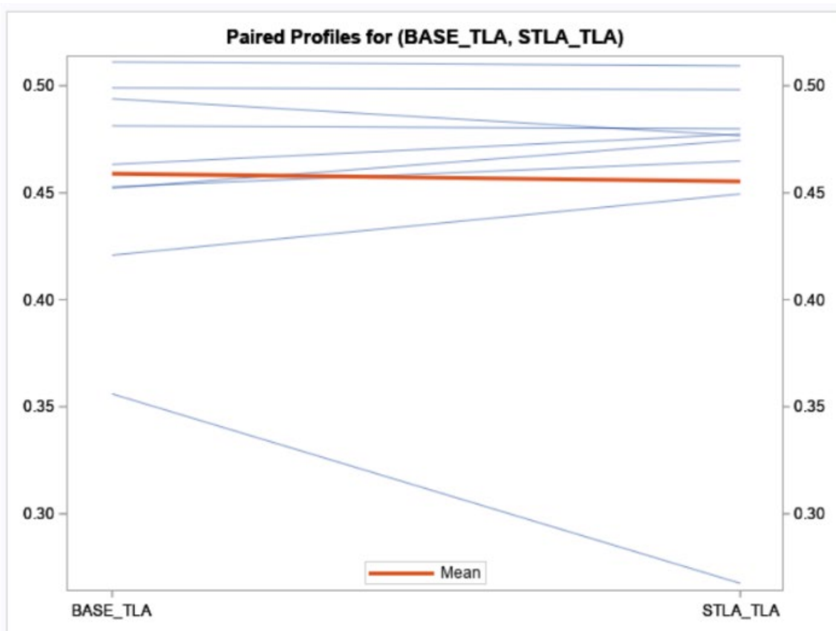
Aim 1: Quantify the effect of trailing limb angle visual feedback on gait symmetry measures in ambulatory individuals with below knee amputation.

In Aim 1 we focused on the use of peak trailing limb angle real time visual feedback on the generation of peak trailing limb angle symmetry (Hypothesis 1), and influence on peak anterior ground reaction force symmetry index (Hypothesis 2) in individuals with below knee amputation while walking on a treadmill.

Aim 1 - Hypothesis 1: *Visual feedback prescribing trailing limb angle symmetry will improve trailing limb angle symmetry.*

Individuals with below knee amputation did not demonstrate a statistical difference in peak trailing limb angle symmetry with the implementation of trailing limb angle real time visual feedback (p=0.76). Several participants (5 of 9: BKA_002, BKA_004, BKA_007, BKA_008, BKA_009) demonstrated increased symmetry with the implementation of visual feedback to encourage peak trailing limb angle symmetry but their small gains in symmetry could not overcome the reduction of symmetry in one subject (BKA_003: Baseline = 0.356 – Symmetry TLA = 0.267) (Figure 14). If that single subject was removed, the data change from Baseline = 0.459 and Symmetry TLA = 0.455to Baseline = 0.472 and Symmetry TLA = 0.479. All subjects are included in our analysis that were able to complete the assessments, thus we cannot exclude BKA_003. There was a small effect (d = 0.11) of visual feedback of trailing limb angle symmetry on the production of trailing limb angle symmetry in individuals below knee amputation (Table 2). This negative effect means that the implementation of real time visual feedback for trailing limb angle symmetry made trailing limb angle symmetry worse in individuals with below knee amputation. (Baseline = 0.459 and Symmetry TLA = 0.455). This was opposite our stated hypothesis for this experiment. The average trailing limb angle symmetry index at Baseline was 0.459, indicating a slightly greater peak trailing limb angle of the intact limb over the prosthetic limb during treadmill walking without visual feedback at self-selected walking speed in individuals with below knee amputation. This relationship between the prosthetic and intact limb did not change with the implementation of real time visual feedback for trailing limb angle symmetry.

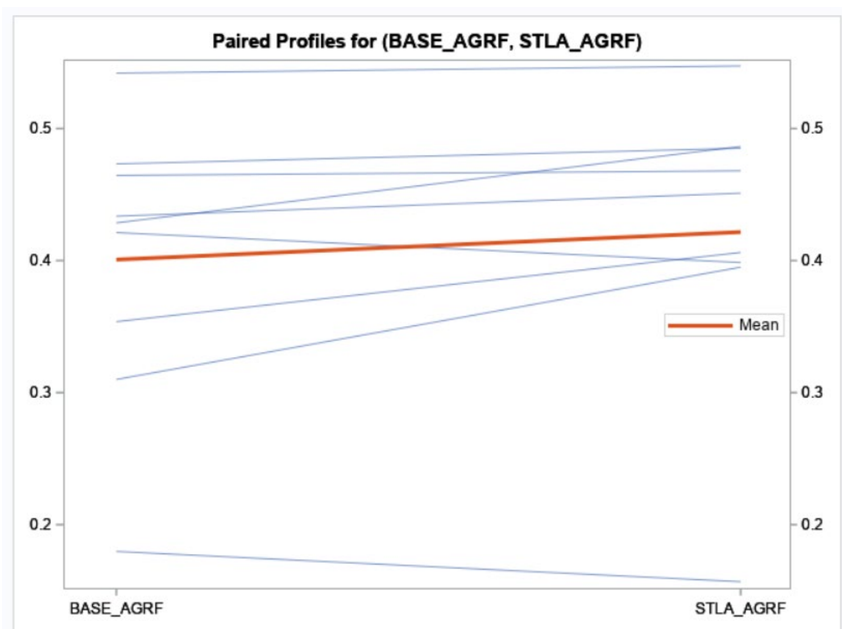
Figure 14: Aim 1 Hypothesis 1: Peak trailing limb angle at Baseline without real time visual feedback (left) and during the trial with symmetry cue for trailing limb angle symmetry (right) in individuals with below knee amputation.



Aim 1 - Hypothesis 2: Visual feedback prescribing trailing limb angle symmetry will improve anterior ground reaction force symmetry.

Individuals with below knee amputation did not demonstrate a statistically significantly different peak anterior ground reaction force symmetry index while walking with real time visual feedback for trailing limb angle symmetry when compared to the baseline trial without visual feedback. (p=0.13). All subjects except three (BKA_001, BKA_003, and BKA_007) demonstrated improved peak anterior ground reaction force symmetry with trailing limb angle symmetry real time visual feedback (Figure 15). All participants except one (BKA_001) had a peak anterior ground reaction force symmetry index at baseline that was less than 0.5 indicating a bias towards the use of their intact limb over their amputated limb. No participants demonstrated a reversal of limb bias during this trial (i.e., limb bias remained unchanged between the Baseline and Symmetry feedback trial for all participants). Three individuals (BKA_001, BKA_003, and BKA_006) demonstrated reduced peak anterior ground reaction force symmetry with visual feedback for trailing limb angle symmetry. The effect of trailing limb angle symmetry real time visual feedback on peak anterior ground reaction force symmetry production was moderate (d=0.6) and in the direction indicating improved ground reaction force symmetry. However, since statistical significance was not achieved, we cannot make meaningful conclusions (Table 2).

Figure 15: Aim 1 Hypothesis 2: Peak anterior ground reaction force symmetry index at Baseline and with trailing limb angle symmetry feedback.



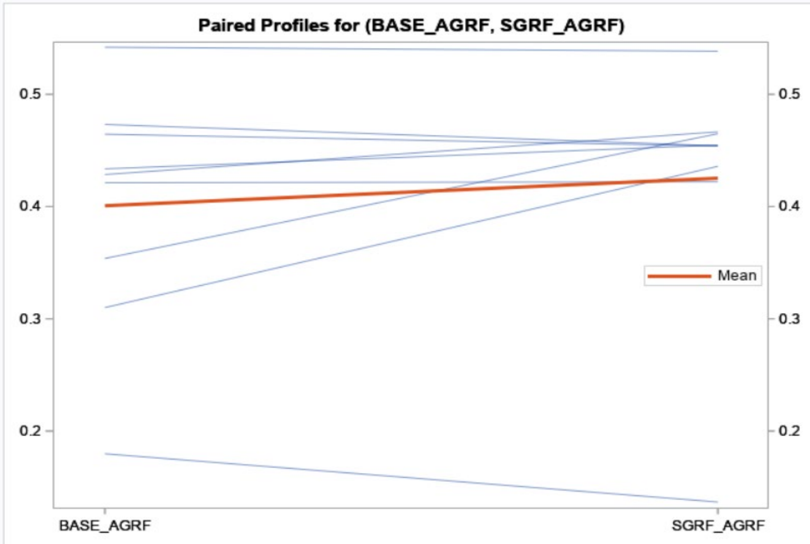
Aim 2: Quantify the effect of anterior ground reaction force visual feedback on gait symmetry measures in ambulatory individuals with below knee amputation.

In Aim 2 we focused on the use of peak anterior ground reaction force real time visual feedback on the generation of peak anterior ground reaction force symmetry (Hypothesis 1), and influence on trailing limb angle symmetry index (Hypothesis 2) in individuals with below knee amputation while walking on a treadmill.

Aim 2 - Hypothesis 1: *Visual feedback prescribing anterior ground reaction force symmetry will improve anterior ground reaction force symmetry.*

There was not a statistically significant effect of peak anterior ground reaction force visual feedback on the generation of peak anterior ground reaction force symmetry in individuals with below knee amputation during treadmill walking (p=0.24). The group mean symmetry improved from 0.40 to 0.43 with the implementation of real time visual feedback for anterior ground reaction force symmetry (Figure 16). All subjects except for one (BKA_001) had baseline and symmetry feedback values of less than 0.5, indicating that most individuals produced a greater amount of propulsive force in the intact limb when compared to the amputated lower extremity. When using the value of 0.5 as symmetry, all but three subjects (BKA_003, BKA_004, BKA_007) demonstrated improved symmetry in peak ground reaction force production using ground reaction force production feedback. Subject BKA_001, even with a baseline asymmetry favoring the prosthetic limb, did show improvement in peak anterior ground reaction force symmetry with anterior ground reaction force visual feedback (SI = 0.542 vs. 0.538). There was a small to medium effect ($d = 0.45$) of peak anterior ground reaction force feedback on the generation of peak anterior ground reaction force symmetry (Table 2).

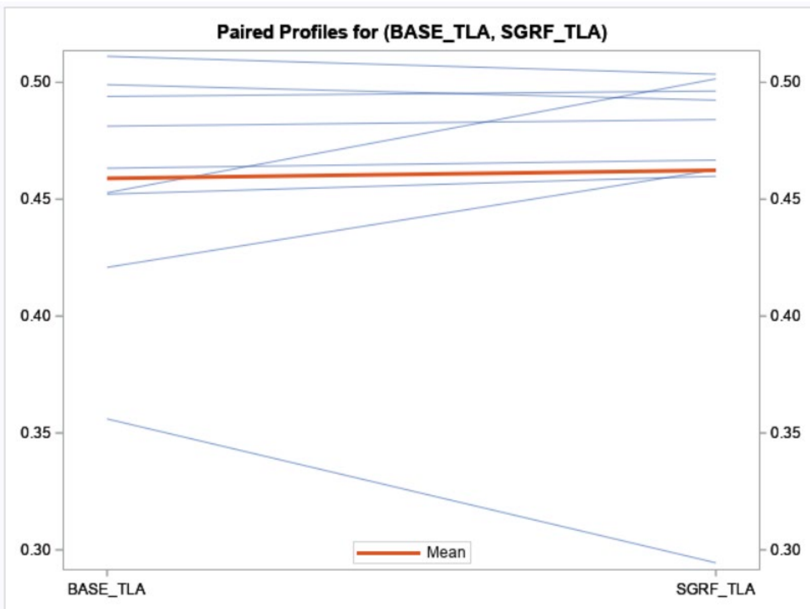
<u>Figure 16: Aim 2 Hypothesis 1:</u> Baseline peak anterior ground reaction force symmetry index and peak anterior ground reaction force symmetry with visual feedback for anterior ground force symmetry. The group average increased from 0.40 to 0.43 indicating an improvement in anterior ground reaction force symmetry.



<u>Aim 2 - Hypothesis 2:</u> Visual feedback prescribing anterior ground reaction force symmetry will improve trailing limb angle symmetry.

There was not a statistically significant difference between the trailing limb angle symmetry during the Baseline trial when compared to the trailing limb angle symmetry during the trial with peak anterior ground reaction force symmetry real time visual feedback. (p=0.75). Seven of the nine participants demonstrated improved trailing limb angle symmetry with the use of real time visual feedback to improve anterior ground reaction force (BKA_002, BKA_004, BKA_005, BKA_006, BKA_007, BKA_008, BKA_009) (Figure 17). One subject (BKA_007) had a trailing limb angle symmetry index indicating greater peak trailing limb angle in the prosthetic limb when compared to the intact limb at Baseline (0.512). Interestingly this same subject (BKA_007) made an improvement in trailing limb angle symmetry index (0.512 to 0.503) though we are not powered to detect and evaluate single subject changes statistically. One subject demonstrated a reversal in limb bias from intact to prosthetic from Baseline to the feedback trial (BKA_008 = 0.45 to 0.501). Two subjects (BKA_001, BKA_003) did not improve their trailing limb angle symmetry with the implementation anterior ground reaction force symmetry visual feedback. Once again one subject (BKA_003) had a potentially negative impact on the group symmetry change. Without participant BKA_003, the change in symmetry index changes from (full data set = 0.458 - 0.462) to (without BKA_003 = 0.471 to 0.483).). Real time visual feedback of peak anterior ground reaction force had a small effect on the production of peak trailing limb angle symmetry (d = 0.1) (Table 2).

<u>Figure 17: Aim 2 – Hypothesis 2:</u> Individual data representation for the change in trailing limb angle symmetry with and without real time visual feedback for anterior ground reaction force production. The group mean increased from 0.459 to 0.462 demonstrating improved trailing limb angle symmetry when prescribing anterior ground reaction force symmetry.



The results of Aims 1 and 2 are summarized in Table 2. As a reminder, successful implementation of visual feedback for all experiments would have resulted in increased symmetry (Symmetry index closer to 0.5 than what was found at baseline). We provide general commentary but not statistical support for whether the symmetry index improved for the group or certain individuals in each experiment. None of the experiments in Aim 1 or 2 were statistically significant for a difference between the two trials. Based on a preliminary review of the Baseline versus the real time visual feedback group averages, it initially appears that Aim 1 - Hypothesis 2 and Aim 2 - Hypotheses 1

& 2 have group average symmetry indices that are closer to symmetry (0.5) then their associated Baseline trial. (Table 2)

Cohen's d effect size was calculated using the standard deviation of the difference between the baseline and intervention conditions.

Table 2: Aim 1 and Aim 2 Statistics Testing summary: None of the completed analyses were statistically significant for any of the hypotheses for Aims 1 or 2. Interlimb symmetry was defined as 0.5. Signs were removed from Cohen's d Effect Size Reporting.

Aim/Hypothesis	**A1H1**	**A1H2**	**A2H1**	**A2H2**
Conditions	**Base_TLA - STLA_TLA**	**Base_GRF - STLA_AGRF**	**Base_AGRF - SGRF_AGRF**	**Base_TLA - SGRF_TLA**
t statistic	**0.31**	**-1.69**	**-1.27**	**-0.33**
p-value	**0.76**	**0.13**	**0.24**	**0.75**
Variable 1 (Avg) [Baseline]	**0.459**	**0.401**	**0.401**	**0.459**
Variable 2 (Avg)	**0.455**	**0.422**	**0.425**	**0.462**
Cohen's d	**0.110**	**-0.599**	**-0.448**	**-0.115**
Effect Size (Small (0.2), Medium (0.5), Large (0.8))	**Small**	**Medium**	**Small - Medium**	**Small**
Goal = Symmetry or Asymmetry	**Symmetry**	**Symmetry**	**Symmetry**	**Symmetry**
Desired Direction? Yes/No	**No**	**Yes**	**Yes**	**Yes**

Table 2a: Pearson Correlations: All objectives in Aim 3 were found to be statistically significant when including all data points for individuals with below knee amputation comparing peak trailing limb angle to peak anterior ground reaction force generation during treadmill walking.

	Pearson's Correlation (Rho)	**p-value**
Aim 3 Objective 1	0.92	0.0004
Aim 3 Objective 2	0.95	<0.0001
Aim 3 Objective 3	0.94	0.0002

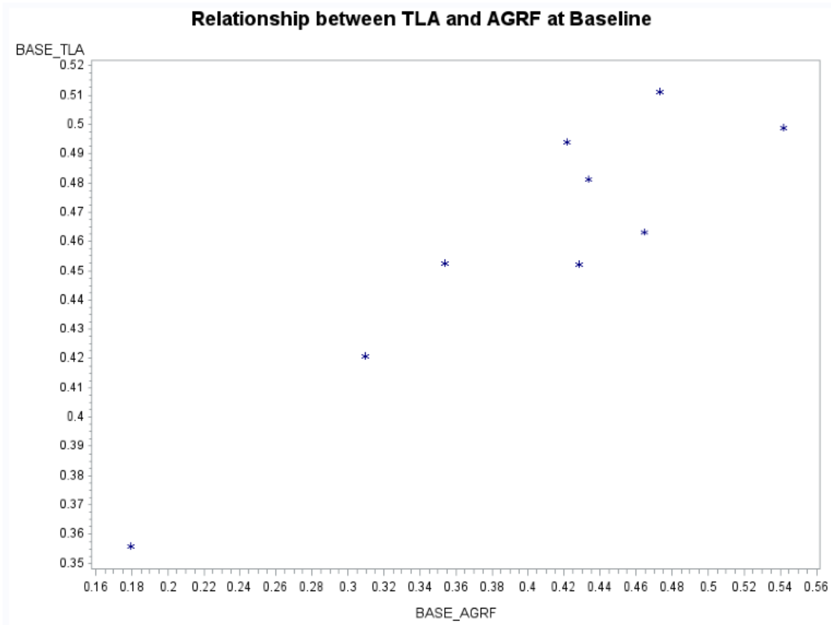
Aim 3: Investigate the relationship between anterior ground reaction force symmetry and trailing limb angle symmetry in individuals with below knee amputation.

Aim three quantified potential correlations between trailing limb angle and peak anterior ground reaction forces. This study was not powered for this exploratory outcome. All three objectives should be interpreted with caution due to the limited number of participants as well as the relatively close grouping with only one apparent outlier. This individual cannot be removed from the analyses because the data points are legitimate and represent a real presentation of an individual with below knee amputation.

> <u>*Aim 3 - Objective 1*</u>*: Quantify the relationship between anterior ground reaction force symmetry and trailing limb angle symmetry when participants walk without visual feedback.*

There was a strong and statistically significant correlation between peak trailing limb angle and peak anterior ground reaction force symmetry in individuals with lower extremity amputation while walking on the treadmill without real time visual feedback (Rho=0.92 and p=0.0004) (Table 2a). During this trial, there was no visual feedback or instruction for levels of symmetry. All available datapoints were included in the correlation, but it is important to notice the potential impact of the individual with particularly low symmetry indices for both trailing limb angle and anterior ground reaction force production (Figure 18). Without good justification the participant's data cannot be removed and are thus included. However, without that single subject, the strength of the correlation remains strong with a resulting Rho=0.79 and p=0.02.

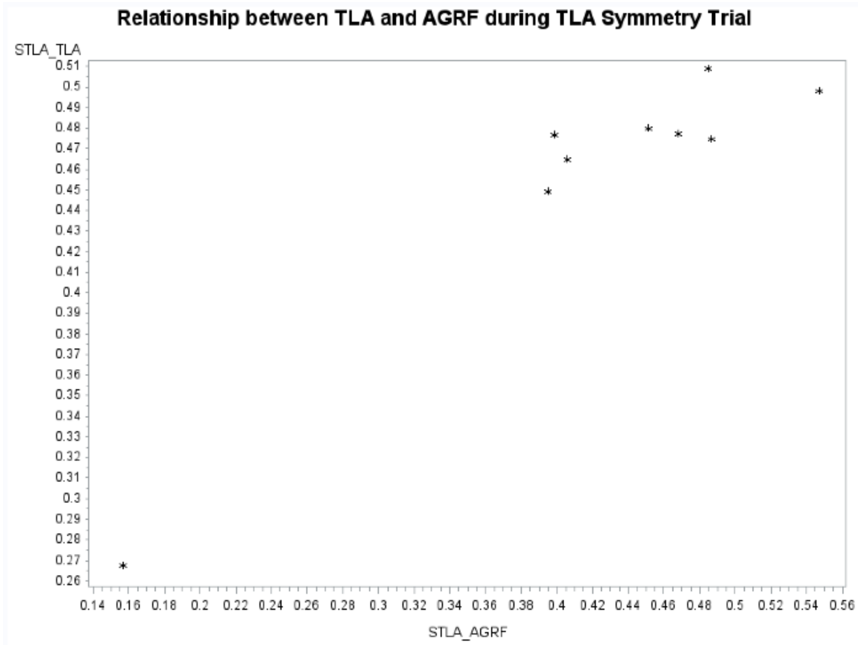
<u>Figure 18: Aim 3 Objective 1:</u> The relationship between peak trailing limb angle and peak anterior ground reaction force in individuals with below knee amputation walking on a treadmill at their self-selected walking speed. Line of best fit is not included at this time due to incomplete participant recruitment.



<u>Aim 3 - Objective 2</u>: Quantify the relationship between anterior ground reaction force symmetry and trailing limb symmetry when prescribing trailing limb angle symmetry.

There was a strong and statistically significant relationship between peak trailing limb angle and peak anterior ground reaction force symmetry indices during treadmill walking with real time visual feedback for trailing limb angle symmetry in individuals with below knee amputation (Rho = 0.95, p=0.0001) (Table 2a). All individuals that were able to complete the trials were included in the analysis. Like what was seen in Aim 3, Objective 1, we observed one participant (BKA_003) that might have a significant impact on the relationship between the two variables even during trailing limb angle symmetry real time visual feedback (Figure 19). We ran the correlation without that individual and found the correlation remains statistically significant, but not as strong (Rho=0.74 p=0.03). This subject remained in the analysis as we do not have a valid physiologic reason for exclusion.

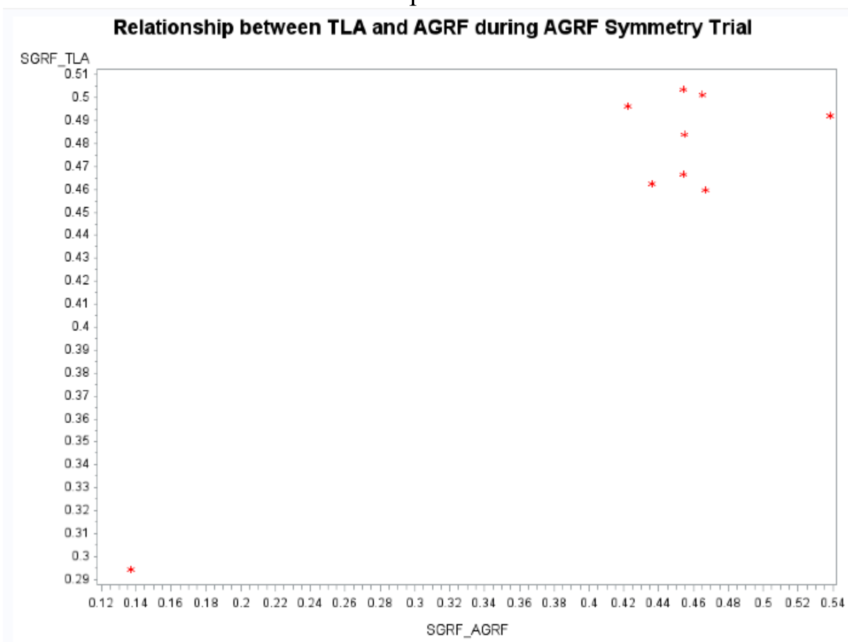
<u>Figure 19: Aim 3 Objective 2:</u> The graphical representation of peak trailing limb angle and peak anterior ground reaction force relationship during treadmill walking with real time visual feedback provided to individuals with below knee amputation during treadmill walking.



<u>Aim 3 Objective 3</u>: Quantify the relationship between anterior ground reaction force symmetry and trailing limb symmetry when prescribing anterior ground reaction force symmetry.

There was a strong and statistically significant correlation between peak trailing limb angle and peak anterior ground reaction force generation during self-selected treadmill walking in individuals with below knee amputation while receiving prescribed real time visual feedback for anterior ground reaction force symmetry (Rho = 0.94, p=0.0002) (Table 2a). Like Objective 2, we sought to uncover a potential relationship between peak trailing limb angle and peak anterior ground reaction force symmetry indices while providing visual feedback. All data points were included for the subjects that completed this objective and a strong correlation was found (Figure 20). Again, the individual with low symmetry indices (BKA_003) for both trailing limb angle and anterior ground reaction force production could impact the correlation seen between the two outcome variables. The correlation does become insignificant when that single subject is removed from the analysis (Rho = 0.15 p=0.73). However, we cannot remove that individual from the analysis because we do not have a valid physiologic reason to believe those values are invalid.

Figure 20: Aim 3 Objective 3: Correlation between peak trailing limb angle and peak anterior ground reaction force production during anterior ground reaction force symmetry real time visual feedback in individuals with below knee amputation.



Aims 4 & 5: Healthy Control Participants

Data presented here focus on the supplemental experiment completed on healthy control participants. All consented participants were enrolled and were able to complete all prescribed study procedures. Data collection was completed on fourteen healthy adults (Mean age = 31 years old), with average height of 170 cm (standard deviation = 11cm) and mass of 74 kg (standard deviation = 9 kg). Participants represented a mix of female and male participants (N=8 and N=6 respectively) although most participants were white, non-Hispanic, (N=13) with right leg dominance (N=13) and none reported any significant past medical history for injuries or surgeries that would impact walking function. Overground unencumbered walking speed averaged 1.32 meters/second (standard deviation = 0.11m/s) and while wearing a solid ankle foot orthosis (SAFO), participants averaged 1.17 meters/second (standard deviation = 0.13 m/s).

Table 3: Demographic Participant Data for Aims 4 & 5: Healthy control demographic and randomization information.

Demographic Information (n=14)	Number/ Mean	%/Std. Dev.
Gender		
Male	6	43
Female	8	57
Race		
Caucasian/White	12	86
Native Hawaiian/ Pacific Islander	1	7
Other	1	7
Black/African American	0	0
Ethnicity		
Hispanic/Latino	1	7
Non-Hispanic/Latino	13	93
Age (years)	31	9
Height (cm)	170	11
Mass (kg)	74	9
Limb Dominance		
Right	13	93
Left	1	7
Overground Walking Speed (m/s)	1.32	0.11
Overground Walking Speed with AFO (m/s)	1.17	0.13
Treadmill Walking Speed (m/s)	0.96	0.15
Treadmill Walking Speed with AFO (m/s)	0.86	0.14
Study Randomization	Number	%
Anterior Ground Reaction Force (AGRF)	8	57
Peak Trailing Limb Angle (TLA)	6	43
Encumbered Limb Randomization	Number	%
Right	8	57
Left	6	43

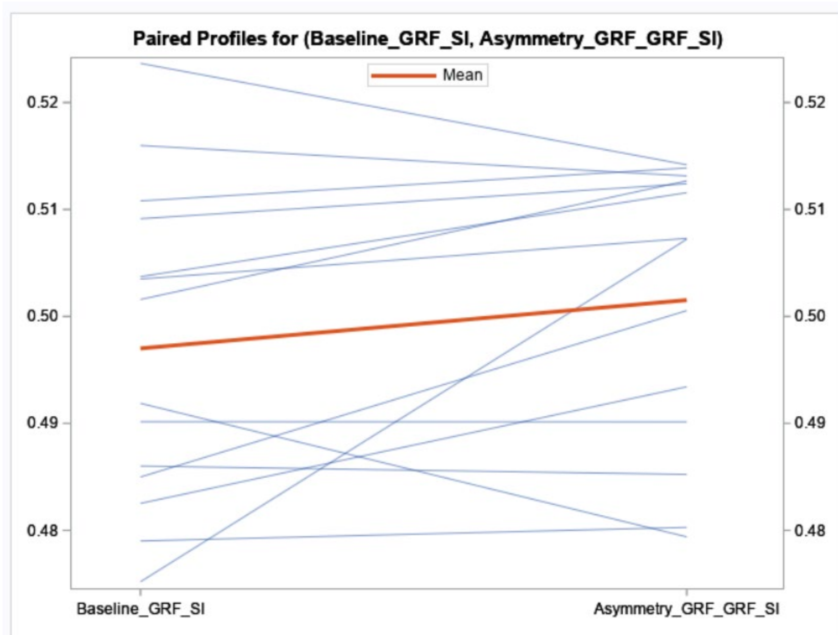
All healthy control participants completed Aim 4 and 5 in sequential order (without solid ankle foot orthosis and then while wearing solid ankle foot orthosis). However, the order of visual feedback was randomized in advance.

Aim 4: Quantify the effect of visual feedback on gait symmetry measures in healthy control individuals. In Aim 4, we tested healthy, unencumbered participants at baseline without real time visual feedback and then again with real time visual feedback to intentionally increase the designated limb's outcome measure (i.e., Trailing Limb Angle or peak Anterior Ground Reaction Force) output by 5% thus generating an asymmetry. This assumed that healthy, unencumbered healthy control participants generate approximately symmetric output of trailing limb angle and anterior ground reaction force at baseline. A total of fourteen participants completed all walking trials and were included in the analysis.

Aim 4 - Hypothesis 1: Visual feedback prescribing anterior ground reaction force asymmetry will increase anterior ground reaction force asymmetry in the unencumbered healthy adult.

There was not a statistically significant difference between the peak anterior ground reaction force symmetry index at Baseline and peak anterior ground reaction force symmetry index during the Asymmetry trial when real time visual feedback for ground reaction force was provided (p=0.15). As a group, the healthy control subjects demonstrated a slight improvement in symmetry (reduction in asymmetry) along with a reversal of which limb generated a greater amount of peak anterior ground rection force (Baseline = 0.49; Asymmetry = 0.501). During baseline walking without visual feedback, half (N=7) of the participants demonstrated a greater use of the experimental leg as opposed to the control leg (Figure 21). The use of real time visual feedback to prescribe increased asymmetry yielded an additional two participants demonstrating experimental limb bias (N=9) during the real time visual feedback trial. Eight of the fourteen subjects demonstrated increased asymmetry over their baseline values during the real time visual feedback trial. There was a small to medium negative effect of the real time visual feedback on the generation of increased asymmetry in the unencumbered healthy control participant ($d = 0.4$) (Table 4). We label the effect as negative because the real time visual feedback decreased the observed peak anterior ground reaction force asymmetry (increased symmetry) from the Baseline trial. Interestingly, the limb preference switched with this effect, a point we will discuss later.

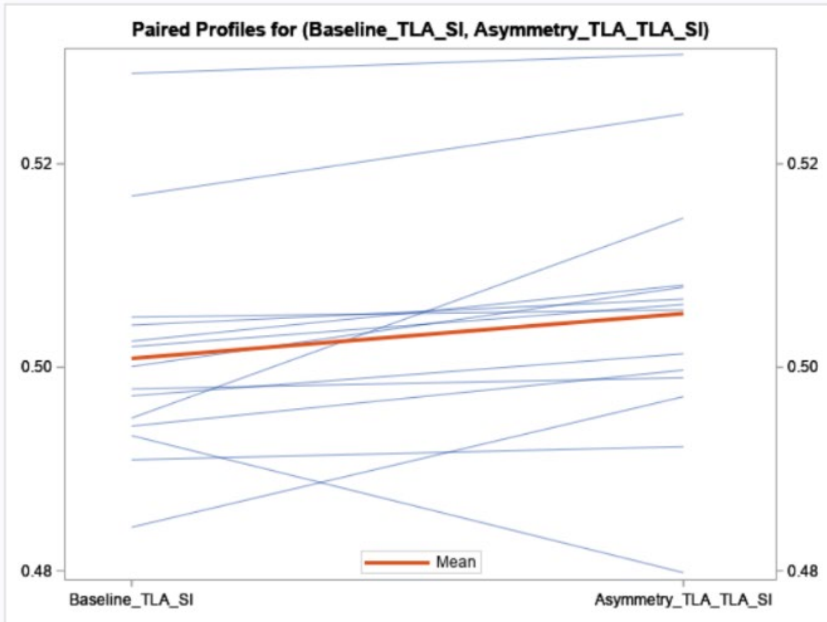
<u>Figure 21: Aim 4 Hypothesis 1:</u> The implementation of a real time visual feedback cue of 5% to increase asymmetry in peak anterior ground reaction force generation in the healthy unencumbered healthy control participant. See Figure 11 for anticipated outcome prior to testing.



<u>Aim 4 - Hypothesis 2</u>: Visual feedback prescribing peak trailing limb angle asymmetry will increase peak trailing limb angle asymmetry in the unencumbered healthy adult.

Unencumbered healthy control subjects demonstrated more asymmetric trailing limb angles when visual feedback was prescribed compared to baseline trailing limb angle asymmetry (p=0.04). The peak trailing limb angle average symmetry index at Baseline for this experiment was 0.50087 indicating near perfect interlimb symmetry (symmetry = 0.50000). When real time visual feedback was provided to increase asymmetry (decrease symmetry) the symmetry index increased to 0.5052 (Figure 22). This is a small to medium positive effect size (d = 0.6) and a statistically significant change (Table 4). In the Baseline trial, exactly half (7/14) participants demonstrated a bias towards the experimental limb, and an additional two subjects (9/14) demonstrated a bias towards the experimental limb during the trial with real time visual feedback to increase trailing limb asymmetry.

<u>Figure 22: Aim 4 Hypothesis 2:</u> Peak trailing limb angle symmetry indices at Baseline and with real time visual feedback prescribing 5% asymmetry. See Figure 11 for anticipated outcome prior to testing.

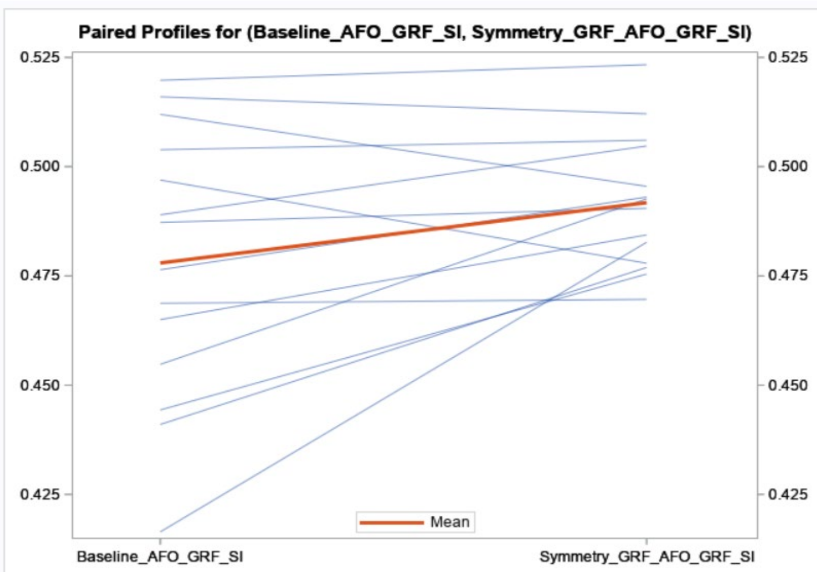


Aim 5: Quantify the effect of visual feedback on gait symmetry measures in healthy control individuals wearing a solid ankle foot orthosis. In Aim 5, healthy control participants were fitted with a solid ankle foot orthosis with the intent of imposing gait asymmetry. They were then prescribed real time visual feedback to encourage symmetry of either trailing limb angle or peak anterior ground reaction force. This Aim was meant to mimic what was completed in hypotheses 1 of Aims 1 and 2.

> *<u>Aim 5 - Hypothesis 1:</u> Visual feedback prescribing anterior ground reaction force symmetry will improve anterior ground reaction force symmetry in healthy adults wearing a solid ankle foot orthosis.*

Healthy control individuals wearing a solid ankle foot orthosis demonstrated a statistically significant difference in peak anterior ground reaction force symmetry with real time visual feedback (p=0.04). Baseline peak anterior ground reaction force asymmetry was observed during this experiment (Mean Symmetry Index = 0.478) with a reduction in asymmetry with the use of visual feedback (Mean Symmetry Index of anterior ground reaction force real time visual feedback = 0.49) (Figure 23). The effect size of the use of real time visual feedback to improve peak anterior ground reaction force was medium (*d* = 0.6) and in the direction indicating improvement of symmetry index. Even while wearing the solid ankle foot orthosis, four individuals demonstrated a bias for the encumbered limb (AAR_021, AAR_026, AAR_029, AAR_030). During the visual feedback trial, three of the four individuals continued to demonstrate a bias towards the encumbered limb, but an additional individual demonstrated bias towards the encumbered limb (AAR_025), and one switched to unencumbered limb bias (AAR_029) (Table 4).

Figure 23: Aim 5 Hypothesis 1: Baseline trial and trial with symmetry feedback for healthy control participants with a solid ankle foot orthosis. Symmetry improved with the use of real time visual feedback.



Aim 5 - Hypothesis 2: Visual feedback prescribing peak trailing limb angle symmetry will improve peak trailing limb angle symmetry in the healthy adult wearing a solid ankle foot orthosis.

Healthy control individuals wearing a solid ankle foot orthosis did not demonstrate a statistically significant difference in symmetry index between the Baseline trial and Symmetry visual feedback trial (p=0.5). Nine of the fourteen participants demonstrated a larger trailing limb angle in the foot wearing the SAFO compared to the control limb during the Baseline trial (Figure 24). During the visual feedback trial, eight of the fourteen participants showed this preference, with a reversal in two subjects from a larger encumbered limb value to control (AAR_021 and AAR_022), and one from control to encumbered (AAR_026). Only five of the participants demonstrated improved symmetry when compared to baseline with the implementation of visual feedback cues for trailing limb angle symmetry (AAR_019, AAR_022, AAR_023, AAR_026, AAR_029). The use of visual feedback to improve trailing limb angle symmetry had a very small effect, but it was in the right direction (*d* = 0.18)

Figure 24: Aim 5 Hypothesis 2: The use of real time visual feedback to improve peak trailing limb angle symmetry in otherwise healthy control participants wearing a solid ankle foot orthosis.

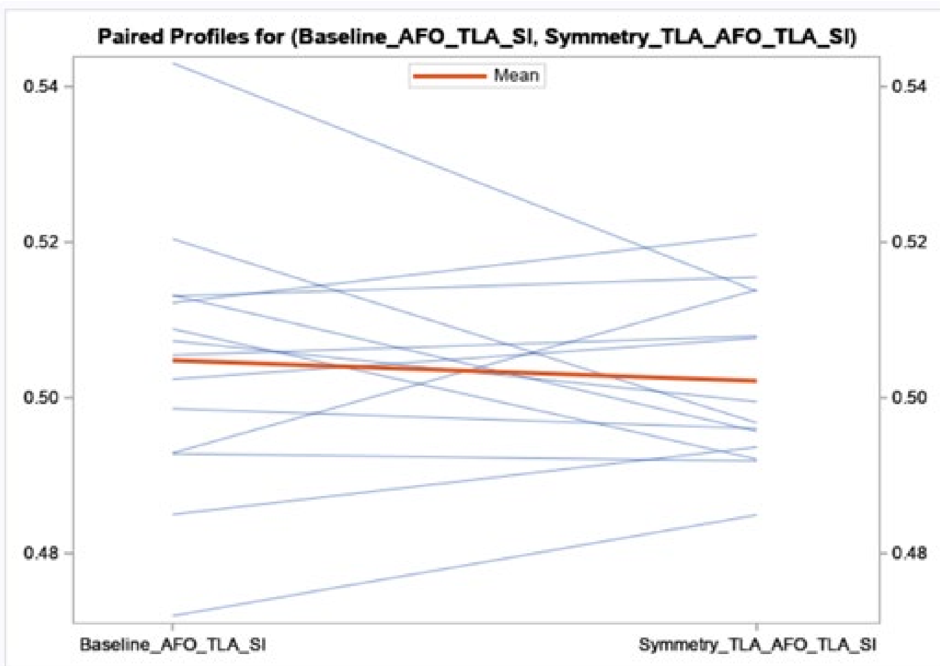


Table 4: Aim 4 and Aim 5 Statistical testing results: Aim 4 and 5 statistics tests results. Effect size was calculated as using the standard deviation of the change scores. *Experiments with statistically significant results.

Aim/Hypothesis	A4H1	A4H2*	A5H1*	A5H2
Conditions	Baseline_GRF_SI – Asymmetry_GRF _SI	Baseline_TLA_SI – Asymmetry_TLA _SI	Baseline_AFO_GRF_SI - Symmetry_GRF_AFO_SI	Baseline_AFO_TLA_SI - Symmetry_TLA_AFO_SI
t statistic	-1.53	-2.26	-2.23	0.68
p-value	0.1488	0.0419	0.0441	0.5098
Variable 1 (Avg) [Baseline]	0.497	0.501	0.478	0.505
Variable 2 (Avg)	0.502	0.505	0.492	0.502
Cohen's d	0.426	0.626	0.618	0.188
Effect Size (Small (0.2), Medium (0.5), Large (0.8))	Small - Medium	Medium	Medium	Small
Goal = Symmetry or Asymmetry	Asymmetry	Asymmetry	Symmetry	Symmetry
Desired Direction? Yes/No	No	Yes	Yes	Yes

Supplemental Analyses

In addition to the primary Aims and hypotheses we explored a few potential relationships and additional variables. We are not powered to detect any differences that we explored and report below and will consider them only exploratory at this time.

Defining Propulsion as Anterior Ground Reaction Force Impulse

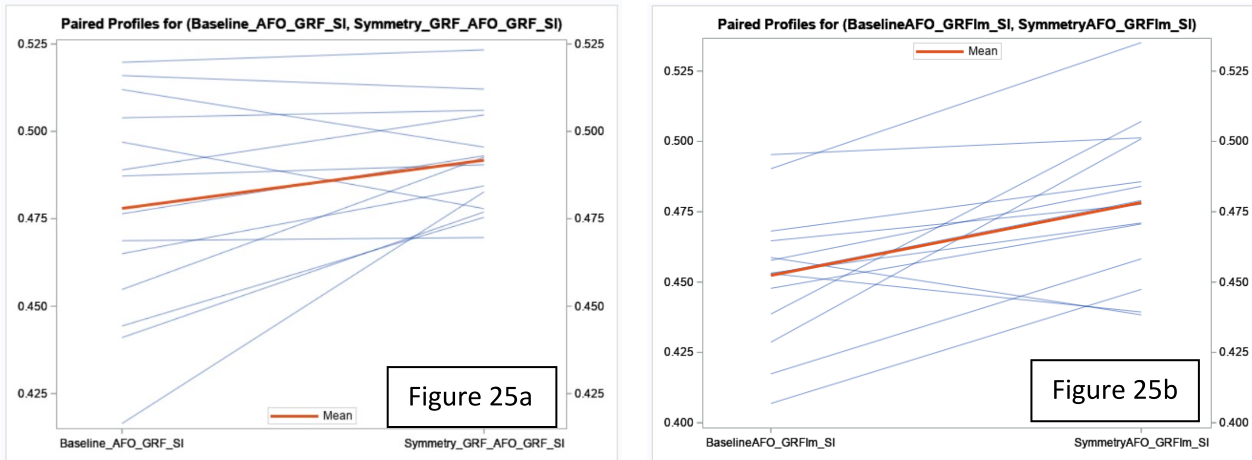
We also analyzed data for trials with peak ground reaction force as the primary outcome measure using anterior ground reaction force impulse. The impulse measure was analyzed for the same segment of the gait cycle as peak anterior ground reaction force (contralateral toe off and ipsilateral mid-stance). When healthy control individuals walked unencumbered using real time visual feedback for peak anterior ground reaction force, there was a near statistically significant difference in anterior ground reaction force impulse generation from baseline (Aim 4 Hypothesis 1 (p=0.0565)). When wearing a solid ankle foot orthosis, there was a statistically significant difference when implementing real time visual feedback to encourage peak anterior ground reaction force symmetry (Aim 5 Hypothesis 1 (p=0.0029)) when compared to the Baseline trial (Table 5).

Table 5: Peak and Impulse Anterior Ground Reaction Force Results: Propulsion can be defined as peak or impulse anterior ground reaction force. Our data show statistical significance in Aim 5, Hypothesis 1. The use of a solid ankle foot orthosis during real time visual feedback to improve symmetry was different for impulse than it was for peak anterior ground reaction force.

		Peak GRF		Impulse GRF	
Aim/Hypothesis	**Conditions**	**t statistic**	**p-value**	**t statistic**	**p-value**
A1H1	Base_TLA - STLA_TLA				
A1H2	Base_AGRF - STLA_AGRF	-1.69	0.1287	-1.31	0.2279
A2H1	Base_AGRF - SGRF_AGRF	-1.27	0.2406	-1.22	0.2586
A2H2	Base_TLA - SGRF_TLA				
A4H1	Baseline_GRF_SI - Asymmetry_GRF_GRF_SI	-1.53	0.1488	-2.09	0.0565
A4H2	Baseline_TLA_SI - Asymmetry_TLA_TLA_SI				
A5H1	Baseline_AFO_GRF_SI - Symmetry_GRF_AFO_GRF_SI	-2.23	0.0441	-3.65	0.0029
A5H2	Baseline_AFO_TLA_SI - Symmetry_TLA_AFO_TLA_SI				

Using impulse instead of peak to quantify anterior ground reaction force to calculate symmetry indices resulted in statistical significance for Aim 5 Hypothesis 1 (p=0.0029); the experiment in which healthy control subjects wore a solid ankle foot orthosis and used real time feedback of peak anterior ground reaction force production to improve peak anterior ground reaction force symmetry. We have presented the two outcome measures for visual inspection and to visualization for healthy control individuals with ankle foot orthosis (Aim 5 Hypothesis 1) (Figure 25). While we present the t-statistic and p-value, the result should be interpreted with care, as the inability to recruit sufficient participants to meet sample size calculations pertains to these data as well.

<u>**Figure 25: Propulsion defined as Peak vs Impulse Anterior Ground Reaction Force:**</u> Peak Anterior Ground Reaction Force (Figure 25a) production for the otherwise healthy control with solid ankle foot orthosis versus Impulse Anterior Ground Reaction Force (Figure 25b). These data are from the participants that completed Aim 5 Hypothesis 1).



<u>Are the individuals with below knee amputation similar to healthy control participants?</u>

During recruitment and enrollment, we made no attempt to match the healthy control participants with the previously enrolled cohort of individuals with below knee amputation in terms of age, gender, or body morphology (height, weight, BMI). However, we make the assertion that there are potential similarities between individuals with below knee amputation to healthy control participants wearing a solid ankle foot orthosis. There were some similarities between the two groups (height, weight, and BMI), and statistically significant differences in other characteristics (Age p=0.00002; Treadmill Speed individuals with below knee amputation versus unencumbered healthy control participants (p=0.00004), Treadmill speed of individuals with below knee amputation versus healthy control participants wearing a solid ankle foot orthosis (p=0.001), overground walking speed of individuals with below knee amputation versus unencumbered healthy control participants (p<0.00001), and overground walking speed of individuals with below knee amputation versus healthy control participants wearing the solid ankle foot orthosis (p<0.00001). In summary, individuals with below knee amputation were older and walked slower on the treadmill and overground when compared to their healthy control counterparts with and without the solid ankle foot orthosis (Table 6).

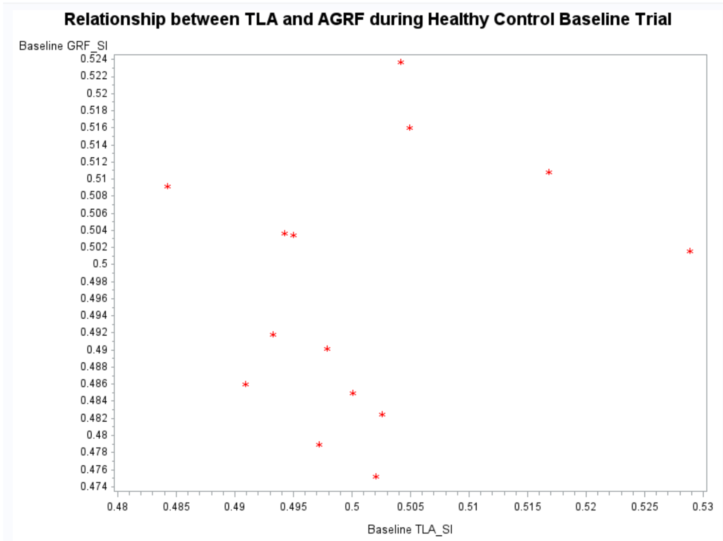
Table 6: Group means and t-test for BKA and Healthy Control participants: Demographic and walking data for individuals with below knee amputation and the healthy control participants that participated in the respective aims in this study. No clinical measures were included in this report.

	BKA Group Average	Healthy Control Average	p-value
Height	175	170	0.279
Weight	85	75	0.141
Age	57	31	0.00002
BMI	27.67	25.96	0.393
Treadmill Speed (m/s)	0.57	0.96	0.00004
Treadmill Speed (m/s) BKA vs AFO	0.57	0.86	0.001
Overground_SSWS (m/s)	0.98	131.67	<0.0001
Overground SSWS (m/s) BKA vs AFO	0.98	117.714	<0.0001

Peak Trailing Limb Angle and Peak Anterior Ground Reaction Force in the Healthy Control Individual

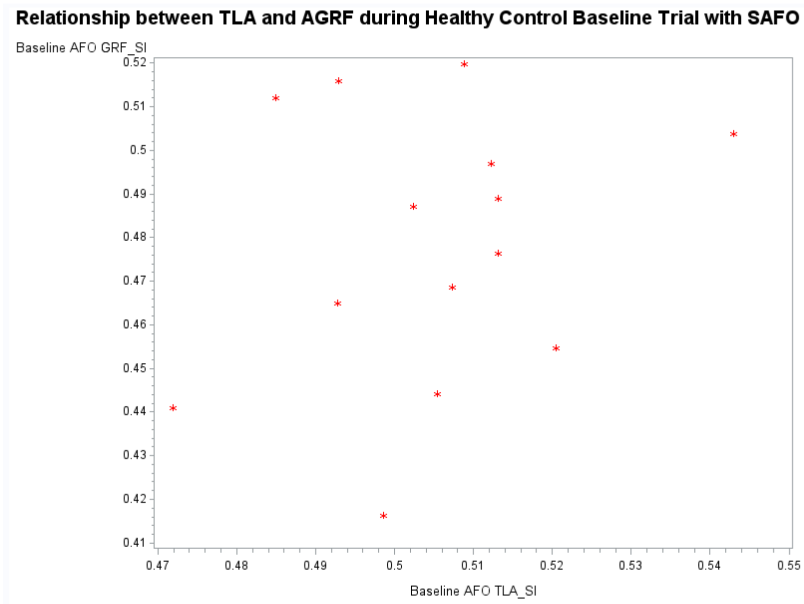
Similar to what we measured in Aim 3 Objective 1, we explored the potential correlation between peak trailing limb angle and peak anterior ground reaction force production in the otherwise healthy unencumbered adult (Figure 26). Unlike individuals with below knee amputation, there was not a significant relationship between the two variables during self-selected treadmill walking without real time visual feedback (Rho = 0.198, p=0.498).

<u>Figure 26: Peak TLA and Peak AGRF correlation in unencumbered healthy adults:</u> During the Baseline trial in otherwise unencumbered healthy controls there was no correlation between the two primary outcome measures. Rho = 0.198, p=0.498

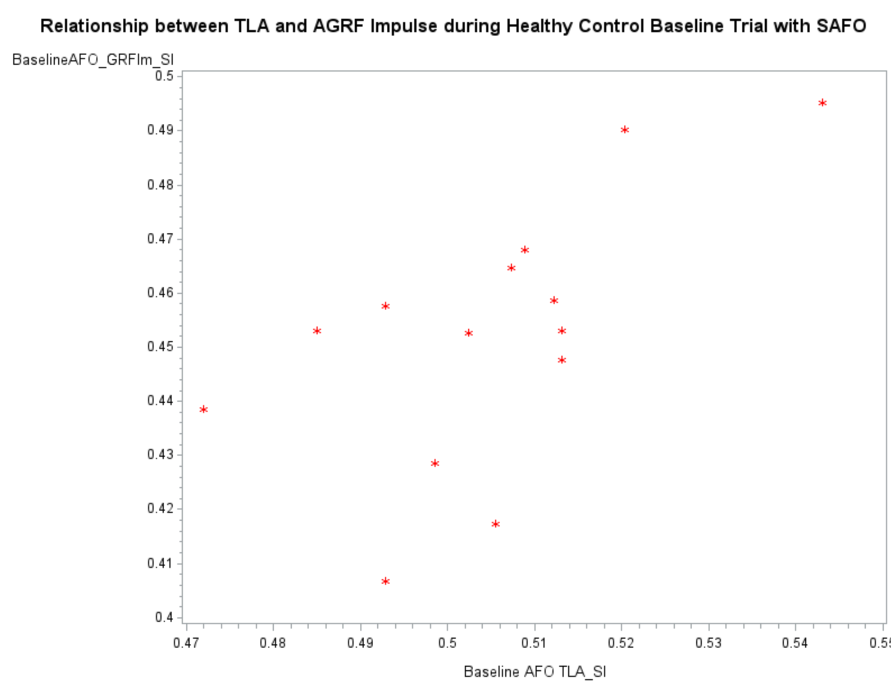


Similarly, the addition of the solid ankle foot orthosis to the otherwise healthy control adult did not result in a significant correlation in healthy controls like what we found in individuals with below knee amputation (Figure 27). The lack of a correlation between peak trailing limb angle and peak anterior ground reaction force generation for encumbered healthy control individuals, changes when using impulse as the measure of propulsion (Rho = 0.628, p=0.016) (Figure 28). This correlation was only explored because of the statistically significant result found in the above supplemental analysis.

<u>Figure 27: Peak TLA and Peak AGRF correlation in healthy adults with SAFO:</u> During the Baseline trial in encumbered healthy controls there was no correlation between the peak trailing limb angle and peak anterior ground reaction force production. Rho = 0.229, p=0.431



<u>Figure 28: Peak TLA and AGRF Impulse correlation in healthy adults with SAFO:</u> During the Baseline trial in encumbered healthy controls there was a statistically significant moderate correlation between the peak trailing limb angle and anterior ground reaction force impulse production. Rho=0.628, p=0.016



Chapter 5: Discussion

Individuals with below knee amputation often present with deficits impacting functional mobility and gait symmetry[13,19,179,181]. We sought to better understand these symmetry deficits, and if they could be modified during steady state treadmill walking using real time visual feedback. Additionally, we supplemented our investigation into symmetry measures in individuals with below knee amputation by collecting data on healthy control subjects with and without a solid ankle foot orthosis to understand the impact of our real time visual feedback and reduced functional movement of the foot and ankle. Our results for experiments completed with individuals with below knee amputation should be interpreted with caution due to incomplete enrollment and inadequate sample size.

In this investigation we used real time visual feedback to elicit changes in symmetry indices of peak trailing limb angle or peak anterior ground reaction force generation in individuals with below knee amputation and healthy control participants with and without encumberment due to a solid ankle foot orthosis. Through this investigation we also explored a potential relationship between peak trailing limb angle and peak anterior ground reaction force in individuals with below knee amputation during steady state walking on a treadmill with and without real time visual feedback. **We found statistically significant differences in only a small number of our experiments. First, trailing limb angle symmetry index was statistically significantly different (an increased trailing limb angle symmetry index from 0.50087 to 0.5052, indicating an increase in trailing limb angle asymmetry) when real time visual feedback for trailing limb angle asymmetry was implemented in unencumbered healthy adults (p=0.04). Next, peak, and impulse anterior ground reaction force symmetry index was statistically significantly different (an increase of peak anterior ground reaction force symmetry index from 0.478 to 0.49 and 0.452 to 0.478**

respectfully, indicating improved symmetry for both measures) when real time visual feedback for anterior ground reaction force symmetry was implemented in healthy adults wearing a solid ankle foot orthosis (p=0.04).

Finally, we also discovered strong positive correlations between peak trailing limb angle and peak anterior ground reaction force generation in individuals with below knee amputation during a Baseline trial (Rho=0.92, p=0.0004, with peak trailing limb angle real time visual feedback (Rho=0.95, p<0.0001), and with peak anterior ground reaction force real time visual feedback (Rho = 0.94, p=0.0002. For all other experiments there were no statistically significant effects of real time visual feedback on symmetry index in individuals with below knee amputation or encumbered or unencumbered healthy control individuals. Effect sizes for all experiments were either small or small to medium and some were not in the direction supporting our hypotheses.

Impact of Real Time Visual Feedback

Real time visual feedback does not appear to consistently change behavior of individuals with below knee amputation or healthy control participants. In our investigation we implemented a custom real-time visual feedback paradigm based on peak anterior ground reaction force or peak trailing limb angle generation. Investigations in the past have used various forms of feedback programs to deliver information directly to an individual to encourage a targeted behavior in a variety of diagnoses[14,21-23,53,54,56,57,192]. However, the use of real time or 'pseudo' real time visual feedback is somewhat limited in individuals with lower extremity amputation[14,52-55]. The feedback we provided was novel. Our feedback was delivered immediately following the termination of each step and disappeared prior to the initiation of the next step on the same side. We did not show aggregate data or any residual from previous step(s) during the trial and instructions were presented to each subject for each trial with verbal acknowledgement of understanding prior to the initiation of the trial. To understand the impact of visual feedback, each trial was compared to the 'Baseline' trial. Like few previously published studies, our feedback program and instructions was to improve or alter symmetry[54], not simply increase trailing limb angle or propulsion[57]. This is important because our primary goal was to determine if the individuals could, by whatever means necessary, generate symmetry. We acknowledge that this may happen in a variety of methods, but here we focus exclusively on if there is an ability to create the desired symmetry and if there is a relationship between peak trailing limb angle and peak anterior ground reaction force production. We tested this in individuals with below knee amputation and healthy control participants with and without solid ankle foot orthosis at baseline, to support a possible link previously published[36,161].

Feedback to Promote Symmetry

All three groups (individuals with below knee amputation, healthy controls, healthy control individuals with solid ankle foot orthosis) were provided feedback with the aim of improving symmetry after some early tests revealed potential asymmetries in trailing limb angle or anterior ground reaction force production among healthy control subjects. The group of individuals with below knee amputations did not contain enough participants to achieve the targeted statistical power. **The effect size was small to medium for all hypotheses, with all but one going in the hypothesized direction.** The resultant effect sizes found in our study generate a power of between 6.5% and 60%. This low power is not ideal and additional work is required before determining if this effect size represents the population of individuals with below knee amputation. Future studies should not use these effect sizes as this might indicate that sample sizes powered at 80% with an alpha of 0.05, would need to be up to 588 participants, making their completion immensely difficult. Our study implemented a form of real time visual feedback on a small and relatively homogeneous group of individuals with below knee amputation.

The real time visual feedback used to promote symmetry may not have been sufficient, targeted, specific enough, or optimal to make meaningful change in kinetic or kinematic gait variables. If the individuals with below knee amputation were not asymmetric 'enough' at baseline it would be unlikely that there would be a significant change or large effect size. However, an aggregate average symmetry index of 0.43 at baseline across both outcome measures, or approximately 14% asymmetry could be improved upon, especially when compared to healthy controls with ankle foot orthosis aggregate baseline symmetry of 0.49, and healthy control aggregate baseline symmetry of 0.5. Finally, the individuals that were able to participate in the data collection process do not represent a wide range of walking speeds and baseline function. Our data begin to support this idea, but additional testing with adequate sample size and power are needed to make a strong statement about this potential correlation. Individuals that walk slowly, have reduced functional capacity and capability, and thus likely exhibit performance impediments such as underlying asymmetries. However, this assumption has not been validated in individuals with below knee amputation.

The method used in this investigation is novel and difficult to compare against other investigations that sought to improve symmetry or increase prosthetic limb output for trailing limb angle or peak anterior ground reaction force. Our investigation contains components (e.g., real time visual feedback on peak trailing limb angle and peak anterior ground reaction force delivered while walking on a treadmill, testing of healthy control participants with a solid ankle foot orthosis, and investigation of the impact of a kinetic variable on a kinematic variable, and the correlation between them) that add to the current body of literature related to walking symmetry with and without impairment or impediment (SAFO). A recent study in able body individuals utilized real time visual feedback using a passive marker system and allowed for participants to hold onto a front handrail during all trials to increase experimental limb output of trailing limb angle or peak anterior ground reaction force during a 60 second walking trial[57]. The investigators then set a target of 25% greater output than what was seen during the Baseline trial. Our experiment used a similar approach of determining a Baseline values for comparison but did so over the entirety of the five-minute trial for individuals with below knee amputation, and two minutes for healthy control individuals (with and without SAFO). The inclusion of all five minutes completed during the Baseline trial allows for the generation of a more stable average outcome measure calculation to reduce step-by-step variability on mean values. We elected for five minutes as the as the duration to provide a "sweet spot" between initial potentially variable walking pattern brought on by a new external challenge and short of a potential impact of exercise induced fatigue[190]. Stated simply, under our laboratory procedures, we start the treadmill and accelerate up to the previously determined self-selected walking speed target, and then as quickly as possible begin data collection to keep walking trials as close to the prescribed length as possible. In our laboratory, some individuals have demonstrated a slight unease in the early portion of a treadmill trial as they become acclimated and have more highly variable stepping performance. We checked for this in post collection processing and only removed steps that were not physiologically possible (e.g., crossover steps). In some clinical populations (e.g., stroke, spinal cord injury, Parkinson's disease) some individuals experience fatigue with prolonged duration walking so staying true to the prescribed walking time is necessary. We were confident, but not certain, that the individuals that were enrolled would not experience this fatigue based on the inclusion/exclusion criteria but know that any clinical population or external construct placed on a healthy control participant, might result in fatigue or mobility disruption. One individual with below knee amputation had difficulty completing the initial five-minute Baseline trial and requested to stop, so an average of what was completed was used (approximately two minutes). Interestingly he was able to complete all subsequent trials as prescribed without difficulty or rest required. Our investigation is of interest because it did not specifically prescribe <u>how</u> participants were to improve their symmetry. Instead, we provided instruction on what was being measured and what the desired outcome for the trial would be (i.e., symmetrical use of both limbs or matching the baseline average). However, our methods are supported because they provide sound foundation that study participants were able to successfully increase peak trailing limb angle and anterior ground reaction force of the experimental limb[57]. Further exploration is required to determine if and how individuals with below knee amputation can alter their peak trailing limb angle and peak anterior ground reaction force (a)symmetry.

The impact of a solid ankle foot orthosis on healthy human control locomotion has not been widely explored. This is likely because a solid ankle foot orthosis is typically only used for a clinical indication of foot drop or a need to control tibial advancement during walking. Our investigation explored the impact of solid ankle foot orthosis as a potential surrogate to understanding the functional impacts of altered gait due to below knee amputation and to begin to understand if it is possible to alter the trailing limb angle and propulsion without a freely functional ankle/foot complex. This is important because the availability of fully mobile joints with sufficient strength in the lower extremity (i.e., hip, knee, ankle) is essential for fully functional and symmetric ‘normal’ bipedal walking. If any major lower extremity joint is impaired, there are kinetic or kinematic consequences on gait mechanics and functional outcomes. In this investigation the underlying assumption was that individuals wearing a solid ankle foot orthosis would not be able to generate any meaningful active plantarflexion contributions to propulsion; a critical component of successful ambulation[37,38,41-43,45,193]. One previous investigation sought to uncover the impact of a SAFO on gait and balance biomechanics under prescribed walking speeds and conditions[25], but did not specifically focus on the relationship of peak trailing limb angle and peak anterior ground reaction force with the use of visual feedback. The use of visual feedback to elicit changes in peak anterior ground reaction force and trailing limb angle symmetry in healthy controls wearing a solid ankle foot orthosis, adds insight about the impact of a SAFO on baseline symmetry during steady state walking, but also, if it is reasonable or realistic to request that an individual with a below knee amputation with prosthesis can alter their kinetic or kinematic output. Our results did not show an overwhelming ability of real time visual feedback to impart meaningful change in symmetry index for either ground reaction force or trailing limb angle for individuals with below knee amputation or healthy control participants that are with or without a solid ankle foot orthosis. We only found that real time visual feedback was able to impact peak trailing limb angle symmetry for unencumbered healthy controls, and anterior ground reaction force production symmetry for healthy controls with a solid ankle foot orthosis. However, the baseline symmetry index for trailing limb angle was already near perfect (Baseline Trailing Limb Angle Symmetry Index = 0.505) and could not be reasonably improved upon using our visual feedback paradigm. Peak anterior ground reaction force in the healthy control group wearing a solid ankle foot orthosis, did demonstrate a level of asymmetry similar to what was found in the baseline trailing limb angle data of individuals with below knee amputation, but not as large as their anterior ground reaction force asymmetry values (Baseline Peak Anterior Ground Reaction Force with SAFO Symmetry Index = 0.48 vs Baseline Trailing Limb Angle for Below Knee Amputee Symmetry Index = 0.46 vs Baseline Peak Anterior Ground Reaction Force for Below Knee Amputee Symmetry Index = 0.4 respectively). While this might indicate that visual feedback for symmetry made this group more asymmetric the effect size is too small and statistical significance is not present to make a meaningful conclusion about the use of real time visual feedback. Our results are consistent with the previous finding of reduced anterior ground reaction force generation when wearing a solid ankle foot orthosis[25] (Table 7).

Feedback to Promote Asymmetry

Based on the notion that healthy control individuals are symmetric, with a reasonable amount of variability, we sought to further support our experimental rationale and uncover whether unencumbered healthy controls could alter their peak anterior ground reaction force and peak trailing limb angle with the visual feedback provided. Prior to initiating this investigation on individuals with below knee amputation and subsequent experiments on healthy controls, unpublished pilot trials were successfully collected to test proof of concept and feasibility of the feedback mechanism. Healthy participants as well as individuals with below knee amputation were able to complete all trials as prescribed and the real time visual feedback worked as described. Post collection analysis demonstrated a data structure conducive to the continuation of this research design and series of experiments. The results generated during pilot testing did not adequately capture the details explored in other aims of this investigation and sought to informally address the ability for the same healthy controls to generate asymmetric peak anterior ground reaction force and trailing limb angle measures.

It is widely assumed that healthy human bipedal gait is ideally symmetric across the lifespan[194]. It is also understood that the healthy neuromuscular system can successfully adapt walking mechanics to meet required demands[17,19,195]. This study is novel in the use of real time visual feedback to elicit asymmetry of peak anterior ground reaction force or trailing limb angle during treadmill walking. Other studies have elected to manipulate the task to measure a change in mechanical output (e.g. increasing treadmill speed to determine step length or propulsion[161]).Our data suggest that the visual feedback provided to our participants did not significantly alter either peak trailing limb angle or anterior ground reaction force symmetry indices. As expected, both outcome measures demonstrated aggregate symmetry at baseline (TLA SI = 0.501; AGRF SI = 0.497), but only trailing limb angle real time visual feedback was able to statistically significantly alter trailing limb angle symmetry. (TLA c Asymmetry Visual Feedback = 0.505; AGRF c Asymmetry Visual Feedback = 0.502). Increasing peak trailing limb angle asymmetry was the more notable outcome. For ease of discussion, we will use the nomenclature control versus experimental limb to indicate limb preference. The control limb did not receive any alteration, where the experimental limb visual feedback was altered to elicit increased output of either peak anterior ground reaction force or trailing limb angle. The experimental limb is the same limb that later wore the solid ankle foot orthosis during that portion of the experiment (previously discussed as the encumbered limb). If the individual demonstrated higher output of the experimental limb relative to the control limb (i.e., SI>0.5), than any increased use of the experimental limb generates an increased symmetry index (e.g., SI = 0.502 -> SI=0.512). If the individual demonstrated higher output with the control limb at baseline (e.g., SI < 0.5), then an increased use of the experimental limb during the trials in which visual feedback for asymmetry was provided, would result in increased symmetry or decreased asymmetry. (e.g., SI = 0.49 -> SI=0.495). Conversely, an individual that demonstrated higher output with the control limb at baseline (e.g., SI <0.5), and subsequently reduced experimental limb output during the asymmetry visual feedback trial would result in increased asymmetry (e.g., SI = 0.49 -> SI = 0.479). Based on our design, underlying assumption, and symmetry index measure, we would have expected to see symmetry index values that were 0.5 at baseline, with an increased asymmetry to a symmetry index greater than 0.5, due to increased utilization of the experimental limb.

When comparing trailing limb angle symmetry index between baseline trial and the trial with visual feedback for asymmetry, all but one subject (thirteen of fourteen subjects) was able to increase their experimental trailing limb angle. Initially this could indicate that our methodology of targeting a single limb to increase output could provide the necessary impetus for alteration of gait symmetry. However, many of the subjects had a baseline trailing limb angle symmetry index that favored the experimental limb. We did not find this directly related to limb dominance but cannot posit due to only one subject with left leg limb dominance in our sample. Thus our results cannot directly support or refute many of the contributions previously made to laterality with respect to symmetry of gait in the healthy control[17]. Of the thirteen participants that increased their experimental trailing limb angle, nine demonstrated increased asymmetry of peak trailing limb angle. One additional participant demonstrated increased asymmetry but did not increase experimental limb trailing limb angle (Baseline Symmetry Index = 0.49; Asymmetry Symmetry Index= 0.48). Two subjects had a reversal of limb dominance for trailing limb angle, but only one of those two was able to increase their asymmetry using the visual feedback provided. These data support the idea that healthy control subjects can make changes in their trailing limb angle output using visual feedback. A plethora of work has been published using visual feedback, but there is no consensus on the exact feedback paradigm to use to promote the most precise alterations of behavioral change during walking. This is one of the first investigations attempting to alter trailing limb angle using visual feedback in healthy control subjects and is encouraging to support the other experiments completed in this investigation. Even if not statistically significant, it is promising to see that healthy controls are able to use the prescribed feedback to alter their behavioral output for peak trailing limb angle symmetry.

When using visual feedback to increase peak anterior ground reaction force asymmetry, similar, but less convincing results are found. Of the fourteen participants, only nine were able to increase the peak anterior ground reaction force of their experimental limb relative to their control. Of the fourteen, a total of eight demonstrated an increase in peak anterior ground reaction force asymmetry. Interestingly three of those nine increased their asymmetry without increasing their experimental limb output. This result is due to the baseline output of the experimental limb in generating the symmetry index. These results, especially considering the trailing limb angle success, become more difficult to interpret. While there is some indication that healthy control individuals wearing a solid ankle foot orthosis can use the visual feedback to alter peak anterior ground reaction force symmetry, and when unencumbered with an AFO can alter their trailing limb angle symmetry, the degree to which this is possible is successful is less promising.

This information is new to the body of literature and should be interpreted with caution. The visual feedback did elicit change in behavioral output for healthy controls, but the degree and magnitude of this change should be further explored.

Relationship of Trailing Limb Angle to Anterior Ground Reaction Force

Our investigation was not explicitly powered to determine correlation between peak trailing limb angle and peak anterior ground reaction force, but it is important to understand how they might interact considering the growing interest in their potential association. It has recently been discovered that there is a direct relationship between our two primary outcome variables (peak trailing limb angle and peak anterior ground reaction force)[35-37,41,57,160,183]. Much of this work has been done with stroke survivors and has generated the possibility of improving symmetry or paretic limb kinetic output (propulsion or anterior ground reaction force) by providing input to, and improving the generation of, a kinematic measure (peak trailing limb angle or hip extension). To date, only a few attempts have been made to investigate a potential relationship between these two primary outcome measures[57,196]. However, Lewek et al. suggests that clinicians consider trailing limb angle as a surrogate measure for propulsive limb forces in stroke survivors[196]. In our investigation, we explored the relationship of these two variables in individuals with below knee amputation with the use of real time visual feedback to promote symmetry as well as during their baseline treadmill walking. Using the data collected during the baseline and feedback trials we were able to determine that there is a relationship between these two variables across the trial types. While we were not powered to detect statistical significance, three correlation coefficients greater than 0.9 indicate a positive correlation for the sample we obtained. This relationship appears somewhat robust, as the correlations remain over 0.9 with visual feedback for anterior ground reaction force symmetry and visual feedback for peak trailing limb angle symmetry provided in separate trials. However, we acknowledge that this finding is likely heavily influenced by a single individual with low peak trailing limb angle and peak anterior ground reaction force symmetry indices. That single subject demonstrated values of trailing limb angle symmetry and peak anterior ground reaction forces that are physiologically possible and likely for this population. By removing the single subject statistical significance remained for two of the three objectives in Aim 3. During self-selected walking without real time visual feedback (Objective 1 p=0.02), and with real time visual feedback of trailing limb angle (Objective 2, p=0.03) a statistically significant correlation was found. This relationship was not maintained during real time visual feedback for peak anterior ground reaction force symmetry index Objective 3, p=0.73). While this may appear to be somewhat robust, we are still cautions to not overstate our results as the sample size and variability of symmetry indices is relatively low. We also know that we did not meet recruitment goals, so it is possible that there are many other individuals that are missing from this dataset. Our findings support recently published data that found an increase in propulsion with trailing limb angle biofeedback as well as anterior ground reaction force feedback[57]. Where our study differs slightly is how we demonstrate this relationship. The previous attempt directly targeted the output of an experimental limb and allowed participants to hold on to an anterior rail. Our approach instructed the participants to generate symmetry based on the visual feedback. The instructions allowed individual flexibility which more likely represents what most bipeds do in determining their steady-state walking pattern and speed[197,198]. This makes interpretation of these findings more complicated and difficult but allows for future post-hoc sub-analyses. For example, individuals might elect to shorten both trailing limb angles to achieve symmetry or decrease push-off or propulsion force on the intact limb to match the prosthetic or figure out another mechanism to increase propulsion or trailing limb angle to match their intact. The effort by Liu et al. helps clarify that it is possible for individuals to alter trailing limb angle and demonstrate a significant alteration of peak anterior ground reaction force production[57].

Our data do not show the same relationship for healthy control participants walking with and without solid ankle orthosis during baseline testing at self-selected walking speed on an instrumented treadmill. The non-statistically significant and very low correlations between peak trailing limb angle and peak anterior ground reaction force in healthy control individuals was Rho=0.19 p=0.498, and for healthy controls with solid ankle foot orthosis the correlation was Rho=0.22, p=0.431. This information does not support the data generated for clinical populations (e.g., stroke and BKA). This is likely due to the relatively tight upper and lower bounds of symmetry indices demonstrated by the healthy control groups both with and without the solid ankle foot orthosis. Additional analyses and adequately powered investigations are warranted to further understand this relationship and the potential implications of altering one or both variables on clinical and behavioral outcomes.

Impulse versus Peak Anterior Ground Reaction Force

In addition to the two primary outcome measures of peak anterior ground reaction force and maximum (peak) trailing limb angle, data were analyzed for the anterior ground reaction force impulse, which incorporates the element of time the force is generated. The results described are an analysis of impulse, but the real time visual feedback was provided as the peak anterior ground reaction force. There were no experimental efforts to use impulse to provide real time visual feedback to any of the participants. The same formula was used to calculate the symmetry index for anterior ground reaction force impulse as was used for peak anterior ground reaction force**. In alignment with the peak anterior ground reaction force data, individuals with below knee amputation did not demonstrate a significant difference from baseline when visual feedback for symmetry of peak anterior ground reaction force was implemented (Table 5).** This is not surprising given the relatively low sample size and somewhat homogenous symmetry production seen in the cohort. This contrasts with the results in the healthy control participants. **The healthy control group without the ankle foot orthosis had a near-statistically significant difference for anterior ground reaction force impulse symmetry index at baseline compared to real time visual feedback for peak anterior ground reaction force asymmetry (Aim 4 Hypothesis 1: p=0.0565). Healthy control participants encumbered by a solid ankle foot orthosis <u>did</u> demonstrate a statistically significant symmetry difference (Aim 5 Hypothesis 1: p=0.0029) when real time visual feedback to improve symmetry was provided.** We recall that the healthy control participants encumbered by a solid ankle foot orthosis also demonstrated a statistically significant difference in peak anterior ground reaction force symmetry index when real time visual feedback for peak anterior ground reaction force symmetry was implemented (p=0.0441).

For unencumbered healthy control participants, we prescribed a goal of increasing asymmetry by generating an increased 5% greater peak anterior ground reaction force in the experimental limb. In this case we note that the symmetry indices for peak change from 0.497 to 0.501 and impulse values change from 0.489 to 0.496. These data indicate that the statistically significant difference in anterior ground reaction force impulse was not in the desired and expected direction (meaning they became more symmetric (closer to 0.5) instead of more asymmetric (away from 0.5)). It is possible that the statistically significant difference is generated by actions of the control or experimental limb by altering the amount of time the limb generated meaningful anterior propulsion.

When healthy control participants wore a solid ankle foot orthosis and were provided real time visual feedback to improve peak anterior ground reaction force symmetry (goal of symmetry index = 0.5) the results were slightly different. In this experiment participants had statistically significantly differences for both peak and impulse symmetry indices for anterior ground reaction force production. This indicates that the changes seen could be due to either magnitude or duration of force anterior force generation. The anterior ground reaction force impulse symmetry index changed from 0.452 to 0.478 and peak from 0.478 to 0.492 from Baseline to real time visual feedback, respectively. These changes were in the desired direction (increased and improved symmetry (i.e., closer to 0.5)) when real time visual feedback was implemented and indicates that healthy control participants wearing a solid ankle foot orthosis can improve ground reaction force symmetry (both peak and impulse) with the use of peak anterior ground reaction force real time visual feedback while walking at self-selected walking speed on a treadmill.

Individuals with Below Knee Amputation - Clinical Measures

The study population of individuals with below knee amputation and healthy control adults was diverse and represented a population of ambulatory individuals capable of completing all required walking trials. The individuals with below knee amputation were all relatively high functioning in terms of K-level as determined by the AMPPro (K4=5, K3=5, K2=1) and thus do not represent the full spectrum of individuals that continue to live with lower extremity limb loss. Of the individuals with below knee amputation that enrolled, there were two that were not included in the full biomechanical analysis: One was classified as K3 and the other a K4. Thus, all the individuals that were included were somewhat limited by the inclusion criteria and study procedures, as they were required to walk without assistance or assistive devices on a treadmill up to five minutes. The data could have been strengthened by the inclusion of a variety of individuals with all possible K-levels, with considerations for reduced levels of mobility.

Our study required individuals to complete all biomechanical analysis trials on a treadmill without upper extremity assistance, thereby creating a selection bias towards higher functioning individuals. This is one of the first areas our design contrasts with other studies of the relationship between trailing limb angle and anterior ground reaction force[36,57,160,183]. By not allowing participants to hold onto handrails or use upper extremity to support themselves during walking trials, we were able to get a true sense of walking function and lower extremity output. This also has the effect of limiting our potential participants, because some individuals with lower extremity amputation might not feel comfortable or safe walking on a treadmill without handrails. Study design likely limited inclusion to individuals with higher K-level classifications as walking on a treadmill can be considered more difficult for individuals with lower limb amputation than walking overground[199] but our study population matches individuals that have participated in similar studies[54,176,178,179,200]. This also aligns the work that relates individuals with higher level K-level functional ambulators to increased Houghton Scores[189].

Our sample was comprised of individuals that scored well on functional mobility, wore their prosthesis regularly, and have faster walking speeds. These individuals demonstrated a relatively high level of walking function (i.e., faster speed, relatively good balance, and functional use of prosthetic devices) and are thereby eligible and likely to have more complex prosthetic technology components. The prostheses worn by all but one of the participants were classified as ESR (Energy Storage and Release), which is a prosthetic foot type typically reserved for more active individuals that would benefit from the design features of energy transference within the device as well as multi-axial design. The multi-axial design of many ESR prosthetic feet requires increased functional mobility and walking ability to successfully balance and properly use the prosthetic foot without negative consequence. However, and somewhat surprisingly, the one participant that walked in a Solid Ankle Cushioned Heel (SACH) foot, a non-ESR foot design, was classified as having a K3 mobility level and demonstrated treadmill and overground walking speeds and outcome measures that were close to the average. This was an interesting finding but not completely surprising because individual preference is a major element of prosthetic foot componentry selection.

A positive consequence of high functional mobility in the enrolled individuals is that there was not any subjective report of fatigue during the investigation. We block randomized trial order a-priori to account for this potential occurrence to mitigate the effects of fatigue on the outcome measures. We also required a minimum of a five-minute rest break between trials to further reduce the likelihood of fatigue impacting our results. Allowing sufficient rest breaks to reduce the impact of fatigue on gait measures in individuals with below knee amputation can be found in formative literature investigating treadmill walking paradigms in individuals with lower extremity limb loss[54,61,201].

Finally, hip and knee active and passive range of motion was assessed for the participants with below knee amputation. There appeared to be a slight limitation in mean active knee extension of the amputated limb compared to the intact limb, but all joints had sufficient passive range of motion to achieve the normal range of motion required for walking[202,203].

Individuals with Below Knee Amputation - Limb Length Considerations

Residual limb length can impact functional gait outcomes across amputation types (above knee versus below knee amputation)[179,204], but this construct is significantly less clear within the cohort of individuals with below knee amputation alone. Residual and intact limb lengths were collected as a potential covariate but were not considered in any supplemental analysis due to no published consensus of short versus long limb length to dichotomize the participants. We explored potential values to split the groups into two equal cohorts, but the **average residual limb length was approximately 43% of the intact length**, with all but two participants falling below the 50% limb length threshold. Discussions with prosthetists and surgeons yield different opinions regarding 'optimal' limb length for individuals with below knee amputation when possible, to choose. However, there was clinical agreement that practical considerations were essential for limb wound closure and healing as well as prosthesis fit. A residual limb too long would be difficult to fit componentry for the prosthesis and could leave tissue that would not properly heal in the case of vascular compromise. A residual limb too short is more difficult to fit a prosthetic socket without hindering proximal joint function and is difficult to close due to the increased volume of proximal soft tissue. Without strict clinical guidelines, it seems to be left to the surgeon and prosthetist team to determine the best residual length for the potential activity level while maximizing healing capacity. There was no analysis performed on outcome measures based on limb length at this time and a larger sample is required to make meaningful correlations.

Walking Speed

The individuals with below knee amputation that completed all components of the experiment had an average overground walking speed of 0.98 m/s and treadmill speed of 0.57 m/s, supporting evidence of reduced walking speed in individuals with lower extremity amputation[205,206]. Based on common interpretations of gait speed functional classification, this group of individuals would be considered to be unlimited community ambulators[207]. We found that participants' mean self-selected a treadmill speed was less than what they performed during overground walking. However, a brief post-hoc review of our data show that the two speeds are strongly correlated (correlation = 0.85). There is some concern regarding the exclusive use of a motorized treadmill to gather and analyze gait patterns of individuals with below knee amputation as the interlimb coordination, temporal symmetry, or joint ranges of motion have been shown to be different[199].

The healthy control group participants walking without the solid ankle foot orthosis presented with near normal walking speeds relative to their age and gender published norms[191]. The average gait speed slowed when wearing the SAFO and when walking on the treadmill, with further reduction in walking speed when walking on a treadmill with a solid ankle foot orthosis combining the two challenges. The use of a solid ankle foot orthosis has been shown to reduce walking speed[31]. This study was not powered to test this interaction or make meaningful conclusions, but we do demonstrate that our study population did show different mean speeds based on the walking context (overground versus treadmill and encumbered versus unencumbered: ($\text{Overground}_{Healthy}$ = 1.31 m/s; Overground_{AFO} = 1.17m/s; $\text{Treadmill}_{Healthy}$ = 0.96 m/s; Treadmill_{AFO} = 0.86 m/s). The healthy control subjects had a faster overground and treadmill gait speed when compared to individuals with below knee amputation. ($\text{Treadmill}_{Healthy}$ = 0.96 m/s, $\text{Overground}_{Healthy}$ = 1.31 m/s vs. Treadmill_{BKA} = 0.57 m/s, Overground_{BKA} = 0.98m/s). While some argue that data collected on a treadmill are similar to overground[208] and others demonstrate significant differences in individuals with lower extremity amputation[199] our data support the idea that the construct matters when analyzing walking of clinical and non-clinical populations. .

The raw difference between treadmill and overground walking speed is greatest among the individuals with below knee amputation (Δ_{BKA} = 0.41m/s; $\Delta_{Healthy\ Control}$ = 0.35m/s; $\Delta_{Healthy\ Controlc\ SAFO}$ = 0.32 m/s). Interestingly the difference between treadmill and overground walking speed average in healthy control individuals wearing a SAFO is the smallest. One possible explanation for this effect is the self-selected walking speed on the treadmill being relatively fast especially when compared to their below knee counterparts. Finally, we note that self-selected walking speed difference between the AFO group on the treadmill and overground is less than that noted between individuals with below knee amputation and unencumbered healthy control participants walking on the treadmill as well as overground (0.28 m/s & 0.2 m/s versus 0.39 & 0.36 m/s respectively). Walking speed is important to consider as it typically contributes directly to measures of propulsion[161,162,178,179]. In our primary analysis, we control for walking speed by using a within subject symmetry index measure that negates the impact of raw speed on propulsion and trailing limb angle. Our investigations only collect data on self-selected walking speed, but increased speed has been shown to increase asymmetry[38,178,179,184,205] and should be considered in future investigations.

Relationship of Overground and Treadmill Walking

Additional data were collected on individuals with lower extremity amputation and healthy control participants while walking overground. **There is a strong correlation (Rho=0.85, p=0.0009) between overground and treadmill walking speed in individuals with below knee amputation.** This correlation is not seen in healthy, unencumbered participants (Rho=-0.05, p=0.85) or healthy control individuals wearing a solid ankle foot orthosis (Rho=0.38 p=0.18). The spatiotemporal measures were not included as primary outcome measures of this study, but here we will discuss some of the most interesting variables collected. We previously discussed overground walking speed and its comparison to treadmill walking. As a reminder we found that healthy, unencumbered participants walked the fastest (group average overground walking speed = 1.3 m/s), followed by healthy control individuals wearing a solid ankle foot orthosis (group average overground walking speed = 1.17 m/s), and finally individuals with below knee amputation (group average overground walking speed = 0.98 m/s). If walking speed is an indicator of overall health or function, these results are logical and expected[45,46]. The difference in overground walking speed between the individuals with below knee amputation and healthy control participants is also somewhat expected when considering participant average age, since the healthy control group was younger (average age = 31 years) than their counterparts with below knee amputation (average age = 57). This compares to published norms for healthy control overground gait speeds of 1.38m/s average for men and women ages 30-39, and 1.37 for men and women ages 50-59. The average overground walking speed for healthy control men and women age 60-69 reduces significantly to 1.29 from the previous decade, which might be a better comparison since the average age for the individuals with below knee amputation is 57. There are a variety of factors that influence walking speed in individuals with below knee amputation, but it appears that one study reports an average of 1.24 m/s for individuals with below knee amputation[209]. However, this average is not stratified by age so we cannot compare our sample to a published average. A logical, yet unverified assumption would assume that older individuals with below knee amputation walk slower than their younger counterparts, and thus our sample might more closely mimic potential normative values. Walking speed is important but is directly influenced by spatiotemporal characteristics like step length.

During overground walking, individuals with below knee amputation demonstrated a mean step length symmetry index average of 0.51. This indicates that there is greater step length of the amputated limb compared to the intact during overground walking with only two participants demonstrating the alternative. This result is potentially interesting especially when considering the trailing limb angle asymmetry result found during treadmill walking. As discussed in the background, step length compromises of two primary components: the distance between the pelvis and the rear foot, and the pelvis to the forward foot. Trailing limb angle is the angle created by the two vectors from the pelvis to the trailing (rear) foot and floor. However, step length is operationally identified by the lead or forward leg. During overground walking, we see a step length that favors a larger distance of the prosthetic step, but not by a large amount. This might support what happens on the treadmill as it 'could' indicate that the prosthetic limb takes a larger step forward or has a smaller trailing limb distance. Even without the ability to fully understand this potential relationship, it is interesting to note that the relative amount of asymmetry found during overground walking for the variable step length is less than that found during treadmill walking for a related variable like trailing limb angle, when the individual can select their own comfortable walking speed without feedback or intervention. Overground symmetry index for step length was similar for the healthy control individuals with and without the solid ankle foot orthosis (0.51 and 0.499 respectively). While these two values are very close to symmetry (0.5), we do note that there is an apparent change in limb preference when walking with (0.51) and without (0.499) the solid ankle foot orthosis. At this time, it is unclear if this is meaningful since we are not powered to detect a change this small in a non-primary variable. This difference from symmetry, likely falls within a normal variance seen for step length in the healthy control. Step length variability has been published as a distance (0.56 +/- 0.94 cm) but not in a symmetry index as we have proposed in this investigation[210].

Baseline Symmetry

This study focused on two symmetry-based outcome measures: Peak trailing limb angle and peak anterior ground reaction force. In all the aims we based our hypotheses on a logical assumption of symmetry or lack thereof depending on the population studied and experimental aim. At the time of study, we were the first to investigate trailing limb angle (a)symmetry in individuals with below knee amputation and its potential relationship to peak anterior ground reaction force production during self-selected treadmill walking. There was no published information on trailing limb angle production or symmetry prior to the initiation of this study, but there are mixed findings regarding asymmetric step length[10,11,13,200], a measure that includes trailing limb angle[13]. Based on published evidence of altered gait measures in individuals with below knee amputation, we assumed trailing limb angle would follow this trend of baseline asymmetric production during unaided walking. One of the metrics known to be asymmetric is propulsion asymmetry or anterior ground reaction force production asymmetry during unaided walking. Reduced ground reaction force production under the prosthetic or amputated limb when compared to the intact limb or healthy control individual's limb for individuals with lower extremity amputation has been previously published[10,19,182,199]. Our findings are similar to what has been published demonstrating asymmetries in both measures

($Baseline_{GRF}$ = 0.4 and $Baseline_{TLA}$ = 0.46), with reduced production from the amputated limb. Analysis of individual subject baseline peak anterior ground reaction forces indicates that all but one subject demonstrated decreased peak anterior ground reaction force from the prosthetic limb when compared to the intact. This outcome is predictable, given the lack of active musculature available to generate propulsive forces at the foot and ankle. What is unclear is how a single subject generated nearly 18% greater peak anterior ground reaction force from his prosthesis when compared to his intact limb. This participant's prosthetic foot manufacturer claims to provide 95% increase in peak ankle power and 82% increased ankle range of motion compared to conventional energy storing and return foot based on design principles[211,212]. We did not test the validity of this claim but acknowledge that the different levels of technology found in more advanced prosthetic foot design may play a role in altering gait kinetics and kinematics of individuals with below knee amputation. Interestingly, anterior ground reaction force impulse follows a similar pattern with even more striking asymmetry (Anterior Ground Reaction Force Impulse Mean Symmetry Index during the Baseline Trial= 0.35) with the same singular subject being the only participate that produced greater force via impulse from the prosthetic limb than the intact. This follows published literature that finds reduced stance time, the key second ingredient alongside peak that produces impulse, for the prosthetic limb compared to the intact[167,213]. In our investigation, trailing limb angle symmetry index in individuals with below knee amputation was also found to be similarly asymmetric at baseline, in line with what we found for peak and impulse anterior ground reaction force symmetry, but far less in magnitude when compared to anterior ground reaction force symmetry. The group average symmetry index for the individuals with below knee amputation was 0.46 with only one participant demonstrating a greater trailing limb angle with the prosthetic limb over the intact (SI = 0.51). What we found is that individuals with below knee amputation have a baseline asymmetry of peak trailing limb angle, peak anterior ground reaction force, and anterior ground reaction impulse production. This result is interesting because it contributes to the discussion about kinematic measurements of individuals with below knee amputation without intervention while walking on a treadmill. This is not overwhelmingly surprising, but further supports the notion that individuals with lower extremity limb loss generally have asymmetries in a variety of kinetic and kinematic variables, even when walking at self-selected speed on a motorized treadmill. And when considering the group of individuals with below knee amputation that were enrolled and completed testing, we can envision that there are likely individuals with greater asymmetries, slower walking speed, and decreased function that might further strengthen this idea. However, we cannot overstate this hypothesis at this time because of our very small sample size and failure to meet stated recruitment goals. Overall step length - which incorporates trailing limb angle as a component[13] - has been shown to be altered in individuals with below knee amputation[176,181]. This also builds on a recently published work that used visual feedback to increase trailing limb angle in healthy control participants but did not report on baseline or post-intervention symmetry indices[57]. Our results provide additional encouragement to assess trailing limb angle and consider the potential effects of asymmetries on gait and mobility in individuals with below knee amputation. The correlation reported between peak trailing limb angle symmetry index and peak anterior ground reaction force in individuals with below knee amputation also potentially implies a potential opportunity to influence a kinematic variable (trailing limb angle) with potentially positive impact on a kinetic measure (propulsion or anterior ground reaction force). The relationship between the two variables at baseline was statistically significant in Aim 3 Hypothesis 1, but in Aim1 Hypothesis 2, and Aim 2 Hypothesis 2, we did not see a statistically significant change in symmetry index of one variable when attempting to change the other (e.g., change in trailing limb angle when visual feedback for anterior ground reaction force symmetry real time visual feedback was provided and vice versa). Thus, the potential impact of a kinetic variable on a kinematic variable (and vice versa) remains to be seen.

Healthy control subjects without a solid ankle foot orthosis appeared to demonstrate better symmetry for both peak anterior ground reaction force and trailing limb angle compared to individuals with below knee amputation (Baseline$_{HCGRF}$ = 0.49 and Baseline$_{HCTL}$ = 0.50). This result was predictable based on the general understanding of bipedal locomotion concepts. This also set the stage for the experiment that aimed to decrease the symmetry of both outcome variables with associated real time visual feedback. When healthy control individuals wore a solid ankle foot orthosis, we demonstrated asymmetry in ground reaction force (both peak and impulse) but no effect of the SAFO on trailing limb angle symmetry (Baseline$_{AFOGRF}$ = 0.477 Baseline$_{AFOIm}$ = 0.45 and Baseline$_{AFOTLA}$ = 0.50). Trailing limb angle has not been investigated in healthy control participants wearing a solid ankle foot orthosis, but our results do partially support evidence of reduced propulsion from the encumbered limb[25]. Peak anterior ground reaction force symmetry indices for healthy adult control participants wearing a solid ankle foot orthosis are similar to what has been demonstrated at a faster walking speeds (1.2 m/s) but differs from that same study in which healthy controls wearing an AFO were found to be symmetric at 0.6 m/s[25]. Our average gait speed was nearly 0.9 (0.87 m/s) which splits the previously published speeds, indicating that the asymmetries in healthy control adults could be different than the 1.2m/s speed value presented by Vistamehr[25]. Our study differs from the Vistamehr study in a few key ways: First, in our investigation individuals wore the solid ankle foot orthosis on either the right or left foot which could have been either the dominant or non-dominant limb; the solid ankle foot orthosis was more tightly secured to the participant during the walking trials with additional wrapping at the superior shank and across the ankle mortis to ensure significant and near complete impairment of ankle movement; and all trials were at the participant's self-selected walking speed (not a pre-determined speed). During self-selected treadmill walking using a solid ankle foot orthosis on one limb, we found asymmetries in ground reaction force production, but not trailing limb angle. The baseline ground reaction force production asymmetry is not surprising, but the lack of trailing limb angle asymmetry is interesting. When walking with a solid ankle foot orthosis, it is not inherently comfortable to put the limb wearing the solid ankle foot orthosis into extension. By limiting or eliminating or eliminating the ability for the ankle to dorsi or plantar flex, the knee is forced to react to this change during self-selected walking. An inability to dorsiflex in terminal stance effectively requires the knee to unlock (flex) in late to terminal stance and mitigates the ability for the limb to actively generate propulsion from the locked ankle. These actions would seem to be incentive enough to not place an encumbered limb (one wearing a well fit solid ankle foot orthosis) in an uncomfortable and disadvantageous position.

During baseline walking for all three participant groups (individuals with below knee amputation, unencumbered and encumbered healthy control participants), baseline (a)symmetries matched our a-priori assumptions except for trailing limb angle symmetry production in healthy control participants wearing a solid ankle foot orthosis. However, if the baseline asymmetries were more pronounced it would increase the potential effect of providing visual feedback. There is some question as to why these asymmetries are not more pronounced in the experimental groups. It is possible that the degree of asymmetries in individuals with below knee amputation would be greater with a broader range of participants and full sample size recruitment, but that remains to be determined. Exactly how individuals determine their self-selected gait kinetics and kinematics and their impact on symmetry remains to be determined.

First, the individuals with below knee amputation or encumbered healthy control participants, might elect to reduce their trailing limb angle on the intact lower extremity to match the prosthetic or encumbered limb to improve their symmetry performance. If the intact or unencumbered limb is generating a greater output of the selected outcome measure than the amputated or encumbered limb, the strategy to produce symmetry as prescribed could be to alter the intact limb instead of the experimental limb. Specific instructions were not provided to the participants about 'how' to alter symmetry. From some additional analyses, we report that the trailing limb angle production in individuals with below knee amputation is less than that generated by individuals with and without solid ankle foot orthosis. The average baseline trailing limb angle is also more asymmetric than their healthy control counterparts with and without solid ankle foot orthosis with a larger average trailing limb angle in the intact limb as opposed to the amputated limb. Furthermore, we observed an average combined trailing limb angle in individuals with below knee amputation that is less than their healthy control counterparts (Table 7). This should be interpreted with caution as walking speed often correlates with hip extension (a likely close correlate to trailing limb angle)[161].

Table 7: Baseline Average Outcome Measure separated by limb and Subject Group: Individuals with below knee amputation demonstrate less trailing limb angle, peak and impulse anterior ground reaction forces for both limbs compared to unencumbered and encumbered healthy control participants. There is also a noted asymmetry at baseline in individuals with below knee amputation of all three variables that is greater than what is seen in the encumbered healthy control participants.

Baseline Trials without real time visual feedback	Baseline Trailing Limb Angle		Baseline Peak Anterior Ground Reaction Force		Baseline Anterior Ground Reaction Force Impulse	
	Prosthetic / Experimental Limb (deg)	Intact Limb (deg)	Prosthetic / Experimental Limb (N/kg)	Intact Limb (N/kg)	Prosthetic / Experimental Limb (N/kg)	Intact Limb (N/kg)
Individuals with Below Knee Amputation	15	17	0.062	0.084	0.013	0.022
Unencumbered Healthy Controls	22	22	0.139	0.142	0.025	0.027
Healthy Controls with SAFO	22	22	0.136	0.140	0.025	0.027

Is walking with a SAFO similar to walking with a prosthesis?

Prior to initiating this study, we used clinical reasoning and logic to posit that an otherwise healthy control individuals wearing a solid ankle foot orthosis might display similar gait kinetics and kinematics when compared to an individual with a below knee amputation. The rationale was rooted in the potential mobility similarity demonstrated at the ankle foot joint of the two groups. There is strong evidence that active plantar flexors are critical to the generation of propulsion via peak and impulse anterior ground reaction force production[38-41,43]. In individuals with below knee amputation and otherwise healthy control subjects wearing a solid ankle foot orthosis, the ability to actively contract the plantar flexors and generate any meaningful propulsion is severely if not entirely limited. There is evidence that a healthy control wearing a solid ankle foot orthosis demonstrates kinetic asymmetries including but not limited to reduced propulsion[25]. There is sound rationale to state that individuals with below knee amputation do not generate propulsive force from an active plantar flexor contraction, because it physically does not exist. Thus, there may be some similarities between these two groups. The selection of the solid ankle foot orthoses to limit ankle plantarflexion was a logical choice given the dearth of evidence involving the use of bracing in an otherwise healthy individual. However, understanding the complexities of prosthetic design, and anterior ground reaction force potentially generated outside of active, reflexive, or volitional contraction of the plantar flexors during the later portion of stance phase of the gait cycle in a healthy control individual, could be more important to understanding the potential relationship between these two groups. Considering the complexities of prosthetic design, our best guess was that the solid ankle foot orthosis would mimic the Solid Ankle Cushioned Heel (SACH) foot with firm heel bumper. Our data did not allow for any group comparisons because the demographic and walking performance difference between the two groups was too great. The healthy control participants were younger, generally more fit (lower BMI), with a faster self-selected treadmill and overground walking speed, and less asymmetric even when encumbered with a solid ankle foot orthosis. However, we did have one subject in each group that could provide some additional insight due to similar speeds as a very small case study. BKA_002 (Individual with below knee amputation) and AAR_030 (Healthy Control with SAFO), had self-selected treadmill walking speeds of 0.55m/s and 0.6m/s, respectively (Table 8). As previously reported, walking speed can impact symmetry[38,178,179,184,205] as well as production of both trailing limb angle (as a component of step length)[161,214] and propulsion[161,162,178,179].

<u>Table 8: A comparison of two similar individuals based on walking speed:</u> Differences between the symmetry indices of two subjects (BKA_002 = individual with below knee amputation; AAR_030 = healthy control participant) with similar walking speed. The individual with a below knee amputation had a self-selected treadmill walking speed of 0.55m/s while the healthy control participant had a self-selected walking speed of 0.6 m/s with and without the solid ankle foot orthosis.

	Baseline AGRF SI	Baseline TLA SI	Overground Step Length SI
BKA_002	0.429	0.452	0.513
AAR_030	0.504	0.543	0.495

This brief example demonstrates (though a very small comparison) that the two individuals were different in their baseline walking symmetry even with nearly identical walking speed. These two individuals did demonstrate overground step length symmetry indices that were more closely matched (BKA_002 = 0.51 vs. AAR_030$_{\text{with SAFO}}$ = 0.495), but the individual with below knee amputation elected to take a longer step with the prosthetic limb (Prosthetic step length = 51.89 cm vs. Intact step length = 49.3 cm). Based on this very small case study, we see that additional investigation with an appropriately powered study needs to occur to consider a healthy control wearing a solid ankle foot orthosis an appropriate surrogate to an individual with a lower extremity amputation.

Considerations across all conditions

Our study design also allowed us to examine a few different possibilities of the impact of visual feedback on individuals with below knee amputation and their healthy control counterparts. We collected identically instructed and matched speed trials at two different time durations: 30 seconds and 5 minutes. We also collected an intermediary trial between the baseline and symmetry cue, in which we provided visual feedback for the participants to match their calculated average peak anterior ground reaction force or peak trailing limb angle generation. With the addition of these trials, we can begin to understand if there is a performance difference perhaps brought on by fatigue, and if there is an impact of simply providing visual feedback to the participants without asking them to alter their gait pattern in any way. A common study design is to use an Analysis of Variance (ANOVA) to examine potential differences within subject across time (i.e., different trial types). For the individuals with below knee amputation, all one-way ANOVA analyses demonstrate some very minor differences across conditions, but none were statistically or clinically significant. Again, these results should be interpreted cautiously. We were not powered to successfully analyze these data using a one-way ANOVA, nor did we meet sample size requirements for our planned analysis. However, the inclusion of these data is important to bring up the lack of standardization in the literature for the analysis of visual feedback implementation. Our approach to the collection, analysis, and presentation of the data represents only one possibility for understanding the impact of visual feedback for tailing limb angle and peak anterior ground reaction force symmetry in individuals with below knee amputation.

Limitations:

It is important to acknowledge some limitations in our work. This work was primarily focused on individuals with below knee amputation and healthy control participants intended to serve as an analogous population when wearing a solid ankle foot orthosis. All presented results should be interpreted with caution. First, we encountered unforeseen circumstances and methodological limitations. These results should only be considered for individuals with below knee amputation as these results are likely different when considering individuals with more involved amputation (e.g., above knee amputation, hemipelvectomy). It is commonly assumed among clinicians that individuals with more significant limb loss demonstrate increased difficulty and reduced symmetry with nearly all aspects of gait, balance, and mobility. Next, the individuals that were able to participate do not necessarily represent the majority of those with below knee amputation since the study required people to walk on a treadmill without upper extremity support or assistance for up to five consecutive minutes. This requirement can be difficult for many individuals that have experienced any type of limb loss, especially when the primary cause of lower extremity limb loss is due to diabetes and peripheral artery disease. The included participants also demonstrated relatively good symmetry at baseline making the utilization of visual feedback to 'improve' these measures of symmetry very difficult to interpret.

The data analysis for individuals with lower extremity amputation was altered as we did not achieve the planned sample size due to difficulty in recruiting potentially available subjects in the community as well as the COVID-19 pandemic during the time of subject recruitment and data collection. Therefore, all data analyses for these Aims did not meet sample size criteria and are underpowered thus potentially resulting in inconclusive results.

The custom feedback program also had some inherent limitations that may have impacted our results. While participants did not complain about the ability to use or understand the output, the ability for the feedback display to consistently show step to step alterations in changes in performance could have been improved to encourage more precise changes in the displayed outcome. For example, when subjects were instructed and provided feedback to improve symmetry, there was no clear guidance on exactly how to improve that symmetry, leaving the individual participant to select the mechanism that best fit the requirement. This limitation can also be considered beneficial for exploratory analyses of exactly how and what choice patterns emerge as potential solutions to the problem of gait asymmetry. This was intentional by design but may have lacked direction that participants may have needed to make meaningful improvements in symmetry outcomes. During Aim 4, the feedback program was initially intended to prescribe a 5% difference in symmetry index, but in fact only calculated a 5% difference in output of the involved limb, which translates to approximately 1-2% change in symmetry index. This very slight change in symmetry, may be within normal variation and too small to make meaningful change. However, this small difference was similar to what was demonstrated by some individuals with below knee amputation, making it an unintentionally beneficial paradigm.

Our results should also be considered only for the impact of visual feedback on treadmill walking. None of the feedback was provided, nor its impact examined during overground self-selected walking. Our data should also be interpreted in the context of a single, self-selected walking speed, without any deviation such as slow, fastest comfortable, acceleration, deceleration, or during stops, starts, turns, or transitional movements.

Finally, the symmetry index utilized was one of several available to us when undertaking this investigation. The interpretation of our findings using this symmetry index was complicated by the ability for the participants to alter their limb preference or dominance. To understand the direction of symmetry, change and attempt to make assertions about directionality, we needed to employ a technique that made it easier to understand the absolute deviation from perfect symmetry. To do this, we calculated the absolute value of 0.5-SI to determine if the reversal of dominance improved symmetry regardless of limb dominance but did not use this in the analysis and reporting. This strategy required individual consideration of each data point for all subjects to ensure proper interpretation. Our selected symmetry index did not have a floor or ceiling effect that we encountered. There is no generally accepted way to present symmetry data in the literature, so comparison of our (a)symmetry findings against other published data should consider how we calculated our measure. It is also unclear if we can fully state there was improved symmetry if individuals increased prosthetic limb output or reduced intact limb output and thereby reversed limb preference during self-selected steady state walking on a treadmill.

Conclusions:

In investigation, we sought to understand the relationship of peak trailing limb angle and anterior ground reaction force relationship as well as the ability for individuals with below knee amputation and healthy control participants with and without solid ankle foot orthosis to use real time visual feedback to alter their symmetry. Individuals with below knee amputation demonstrate propulsion asymmetry (as defined by both peak and impulse) at baseline without the implementation of real time visual feedback. The use of real time visual feedback for either peak trailing limb angle or peak anterior ground reaction force symmetry prescription did not result in any statistically significant changes in symmetry indices, but a positive correlation between the two outcome measures was found with and without visual feedback. In additional work, we mimicked the experience provided to individuals with lower extremity amputation, in healthy control individuals with and without a solid ankle foot orthosis. The otherwise healthy unencumbered adults demonstrated statistically significant differences trailing limb angle symmetry index when corresponding visual feedback was provided. This did not occur with the provision of peak anterior ground reaction force visual feedback on peak anterior ground reaction force symmetry index. When the healthy control individuals were fitted with a solid ankle foot orthosis, they were able to demonstrate statistically significant change in peak anterior ground reaction force symmetry index with the corresponding real time visual feedback. This difference was not found for peak trailing limb angle when real time visual feedback for trailing limb angle symmetry was prescribed. The data provide insights to potential relationships between kinetic and kinematic variables during self-selected treadmill walking of individuals with below knee amputation, but further investigation of the provision of real time visual feedback to alter symmetry is needed. The addition of the healthy control participants did not further clarify the real time visual feedback paradigm, nor did it strongly resemble individuals with below knee amputation. Additional study is needed to investigate the concepts of real time visual feedback, kinetic and kinematic symmetry, and the relationships between these variables in individuals with below knee amputation as well as their encumbered and unencumbered otherwise healthy control counterparts.

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Appendices:

<u>Appendix A:</u> Data Collection Sheet for Aims 1-3

Data Collection Sheet

Study Name: The use of pseudo real-time visual feedback to alter anterior ground reaction force and trailing limb angle symmetry in the below knee amputee

Study Subject ID: ____________________ Date of Assessment: ______________

Study Staff: ____

Check list:
_____Turn on and zero Bertec Treadmill
_____Turn on and calibrate Phase Space
_____Full Lower Body Marker set up
_____Demographic Data Collected
_____Clinical Tests completed: ____GaitRite / _____AmpPro / _____Houghton Scale

Order (Random)	Trial #	Trial Name	Duration	Notes:
	______	Static		
	______	Walking Speed Test	30 seconds	
		TM SSWS: _____________		
		Pre: Blood Pressure / Heart Rate		
	______	Baseline (BASE)	5 Minutes	
		Blood Pressure / Heart Rate		
	______	Matched Baseline - TLA (VIDEO-TLA)	5 Minutes	
		Blood Pressure / Heart Rate		
	______	Symmetry Target - TLA (TARGET-TLA)	5 Minutes	
		Blood Pressure / Heart Rate		
	______	Matched Baseline - GRF (VIDEO-GRF)	5 Minutes	
		Blood Pressure / Heart Rate		
	______	Symmetry Target - GRF (TARGET-GRF)	5 Minutes	
		Blood Pressure / Heart Rate		

Baseline Values		
	Left	Right
AGRF		
TLA		

Appendix B: Data Collection Sheet for Aims 4 & 5

Demographic Table		**Frequency/Median**
Gender (M/F)		
Age(yr.)		
Time since amputation (mo.)		
Cause of Amputation		
	Traumatic	
	Non-trauma - Vascular	
	Non-trauma - Cancer	
	Non-trauma - Congenital Defect	
Foot Type		
	Microprocessor	
	ESR	
	SACH	
Limb involved (L/R)		
Houghton Scale (0-12)		
AMPPRO Score (15-47) Overground SSWS (m/s)		

<u>Appendix C:</u> Amputee Mobility Predictor

1. Sitting balance: sit forward in a chair with arms folded across chest for 60s.	Cannot sit upright independently for 60s Can sit upright independently for 60s	=0 =1	
2. Sitting reach: reach forward and grasp the ruler. (Tester holds ruler 12in beyond extended arms midline to the sternum.)	Does not attempt Cannot grasp or requires arm support Reaches forward and successfully grasps item	=0 =1 =2	
3. Chair to chair transfer: 2 chairs at 900. Pt may choose direction and use their upper extremities.	Cannot do or requires physical assistance Performs independently, but appears unsteady Performs independently, appears to be steady and safe	=0 =1 =2	
4. Arises from a chair: ask pt to fold arms across chest and stand. If unable, use arms or assistive device.	Unable without help (physical assistance) Able, uses arms/assist device to help Able, without using arms	=0 =1 =2	
5. Attempts to arise from a chair (stopwatch ready): if attempt in no. 4was without arms then ignore and allow another attempt without penalty.	Unable without help (physical assistance) Able requires >1 attempt Able to rise 1 attempt	=0 =1 =2	
6. Immediate standing balance (first 5s): begin timing immediately.	Unsteady (staggers, moves foot, sways) Steady using walking aid or other support Steady without walker or other support	=0 =1 =2	
7. Standing balance (30s) (stopwatch ready): For items nos. 7 & 8, first attempt is without assistive device. If support is required, allow after first attempt.	Unsteady Steady but uses walking aid or other support Standing without support	=0 =1 =2	
8. Single-limb standing balance (stopwatch ready): time the duration of single limb standing on both the sound and prosthetic limb up to 30s. Grade the quality, not the time.	Nonprosthetic side Unsteady Steady but uses walking aid or other support for 30s Single-limb standing without support for 30s	 =0 =1 =2	
Sound side ____seconds Prosthetic side ____seconds	Prosthetic Side Unsteady Steady but uses walking aid or other support for 30s Single-limb standing without support for 30s	 =0 =1 =2	
9. Standing reach: reach forward and grasp the ruler.(Tester holds ruler 12in beyond extended arm(s) midline to the sternum.)	Does not attempt Cannot grasp or requires arm support on assistive device Reaches forward and successfully grasps item no support	=0 =1 =2	
10. Nudge test (subject at maximum position #7): with feet as close together as possible, examiner pushes firmly on subject's sternum with palm of hand 3 times (toes should rise).	Begins to fall Staggers, grabs, catches self, or uses assistive device Steady	=0 =1 =2	

11. Eyes closed (at maximum position #7): if support is required grade as unsteady.	Unsteady or grips assistive device	=0
	Steady without any use of assistive device	=1
12. Picking up objects off the floor (pick up a pencil off the floor placed midline 12in in front of foot).	Unable to pick up object and return to standing	=0
	Performs with some help (table, chair, walking aid, etc)	=1
	Performs independently (without help from object or person)	=2
13. Sitting down: ask pt to fold arms across chest and sit. If unable, use arm or assistive device.	Unsafe (misjudged distance, falls into chair)	=0
	Uses arms, assistive device, or not a smooth motion	=1
	Safe, smooth motion	=2
14. Initiation of gait (immediately after told to "go").	Any hesitancy or multiple attempts to start	=0
	No hesitancy	=1
15. Step length and height: walk a measured distance of 12ft twice (up and back). Four scores are required or 2 scores (a & b) for each leg. "Marked deviation" is defined as extreme substitute movements to permit clearing the floor.	a. Swing foot	
	Does not advance a minimum of 12in	= 0
	Advances a minimum of 12in	= 1
	Prosthesis Sound	
b. Foot clearance	Foot does not completely clear floor without deviation	= 0
	Foot completely clears floor without marked deviation	= 1
	Prosthesis Sound	
16. Step continuity.	Stopping or discontinuity between steps (stop & go gait)	= 0
	Steps appear continuous	= 1
17. Turning: 1800 turn when returning to chair.	Unable to turn, requires intervention to prevent falling	= 0
	Greater than 3 steps but completes task without intervention	= 1
	No more than 3 continuous steps with or without assistive aid	= 2
18. Variable cadence: walk a distance of 12ft fast as safely as possible 4 times. (Speeds may vary from slow to fast and fast to slow, varying cadence.)	Unable to vary cadence in a controlled manner	= 0
	Asymmetrical increase in cadence controlled manner	= 1
	Symmetrical increase in speed in a controlled manner	= 2
19. Stepping over obstacle: place a movable box of 4in. in height in the walking path.	Cannot step over the box	= 0
	Catches foot, interrupts stride	= 1
	Steps over without interrupting stride	= 2
20. Stairs (must have at least 2 steps): try to go up and down these stairs without holding on to the railing. Don't hesitate to permit pt to hold on to rail. Safety first, if examiner feels that any risk in involved omit and score as 0.	Ascending	
	Unsteady, cannot do	= 0
	One step at a time, or must hold on to railing or device	= 1
	Steps over step, does not hold onto the railing or device	= 2
	Descending	
	Unsteady, cannot do	= 0
	One step at a time, or must hold on to railing or device	= 1
	Steps over step, does not hold onto the railing or device	= 2
21. Assistive device selection: add points for the use of an assistive device if used for 2 or more items. If testing without prosthesis use of appropriate assistive device is mandatory.	Bed bound	= 0
	Wheelchair	= 1
	Walker	= 2
	Crutches (axillary or forearm)	= 3
	Cane (straight or quad)	= 4
	None	= 5

	AMPPro	AMPnoPro
K0	N/A	0-8
K1	15-26	9-20
K2	27-36	21-28
K3	37-42	29-36
K4	43-47	37-43

Total Score 0 /47

K level =

Trial ☺ no prosthesis ☺ with prosthesis Observer

Date

Abbreviation: PF, partial foot; TT, transtibial; KD, knee disarticulation; TF, transfemoral; HD, hip disarticulation; Pt, patient.

Content has been exerpted from Gailey RS, Roach KE, Applegate EB, et al. The amputee mobility predictor: an instrument to assess determinants of the lower-limb amputee's ability to ambulate. *Arch Phys Med Rehabil*. 2002;83(5):613-627.

Appendix D: Houghton Scale

Houghton Scale

1: Do you wear your prosthesis:

- 0- Less than 25% of waking hours
- 1- Between 25% and 50% of waking hours
- 2- More than 50% of waking hours
- 3- All waking hours

2: Do you use your prosthesis to walk:

- 0- Just when visiting your doctor or limb-fitting center
- 1- At home but not to go outside
- 2- Outside the home on occasion
- 3- Inside and outside at all times

3: When going outside wearing your prosthesis, do you:

- 0- Use a wheelchair
- 1- Use two crutches, two canes, or a walker
- 2- Use one cane
- 3- Use nothing

4: When walking with your prosthesis outside, do you feel unstable when:

4a) Walking on a flat surface

0- Yes 1-No

4b) Walking on slopes

0- Yes 1-No

4c) Walking on rough ground

0- Yes 1-No

Houghton Score Categories

It defines community and household walking ability.

- Houghton Scale score ≥ 9- independent community
- Houghton Scale scores 6–8- household and limited community
- Houghton Scale score ≤ 5- limited household

<u>Appendix E:</u> Demographic Data Collection Sheet for Individuals with Below Knee Amputation

<u>Demographic Table</u>	
Testing Date	
Subject ID Number	
Gender	M / F
Race	AA / A / AI / H / C / O
Ethnicity	Hispanic / Non-Hispanic
Height (cm)	
Weight (with prosthesis) lbs.	
DOB (Month/Yr.)	
Age at time of testing (Years)	
Date of Amputation (Month/Yr.)	
Time since Amputation (Months)	
Amputation Etiology	Traumatic / Non-Trauma-Vascular / Non-Trauma-Cancer / Non-Trauma-Congenital Defect / Elective Other
Prosthesis Components	
Socket Suspension Type	
Pylon Type	
Foot	
Sock Ply during testing	
Prosthetist Company / Provider	
Amputated Limb (Involved)	L / R
Houghton Scale Score (0-12)	
AMPPro Score (15-47) / K-level	
Overground SSWS (m/s)	
Limb Length Amputated (Tibia)* (cm)	
Limb Length Intact * (cm)	
<u>Involved</u> Hip Range of Motion (passive)	Flexion ______________ Extension_____________
<u>Involved</u> Hip Range of Motion (ACTIVE)	Flexion ______________ Extension_____________
<u>Involved</u> Knee Range of Motion (passive)	Flexion ______________ Extension_____________
<u>Involved</u> Knee Range of Motion (ACTIVE)	Flexion ______________ Extension_____________

Consent and HIPAA Date: ____________________

*Note: Limb length intact is measured from lateral joint line to lateral malleolus. Amputated limb length is measured from the bisection of the anterior joint line of the knee to the distal end of the residual limb.

<u>Appendix F:</u> Demographic Data Collection Sheet for Healthy Control Participants

<u>Demographic Table</u>	
Testing Date	
Subject ID Number	
Gender	M / F
Race	AA / A / AI / H / C / O
Ethnicity	Hispanic / Non-Hispanic
Height (cm)	
Weight (lbs.)	
DOB (Month/Yr.)	
Age at time of testing (Years)	
Overground SSWS (m/s)	
Limb Length Intact * (cm)	
<u>Involved</u> Hip Range of Motion (passive)	Flexion ____________ Extension____________
<u>Involved</u> Hip Range of Motion (ACTIVE)	Flexion ____________ Extension____________
<u>Involved</u> Knee Range of Motion (passive)	Flexion ____________ Extension____________
<u>Involved</u> Knee Range of Motion (ACTIVE)	Flexion ____________ Extension____________

Consent and HIPAA Date: ____________________

*Note: Limb length intact is measured from lateral joint line to lateral malleolus. Amputated limb length is measured from the bisection of the anterior joint line of the knee to the distal end of the residual limb.

Appendix G: IRB Approved Study Advertisements

IRB Number: Pro00082064
Date Approved 6/26/2019

MUSC
Medical University of South Carolina
Changing What's Possible

Study Explanation

Walking after a lower extremity amputation is often difficult. It is important that researchers and clinicians understand the mechanisms that inhibit normal walking function. In this study, we are recruiting individuals with lower extremity limb loss for a walking and balance investigation.

PI: Aaron E. Embry, PT, DPT, MSCR

Contact us today if you are interested in participating in this research opportunity!

MUSC
Medical University of South Carolina
Changing What's Possible

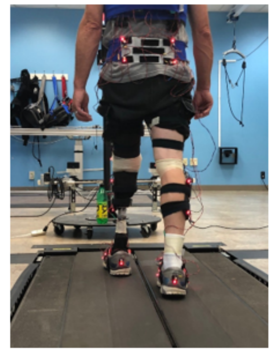
Contact: Aaron Embry

Office: 843-792-8198

embry@musc.edu

Below Knee Amputee Gait and Mobility

MUSC IRB Pro#00082064



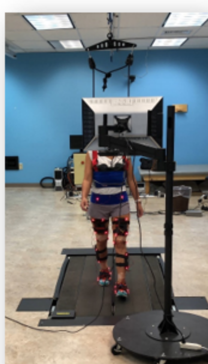
A research study opportunity for individuals with lower extremity amputation.

IRB Number: Pro00082064
Date Approved 8/7/2019

MUSC
Medical University of South Carolina
Changing What's Possible

The Process

1) Written informed consent
2) Clinical assessments
3) Biomechanical assessment



All procedures are typically completed in a single visit lasting approximately 3 to 3.5 hours.

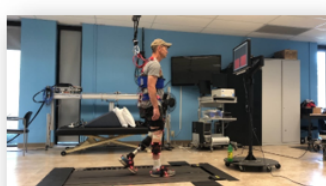
Am I eligible?

1) Unilateral lower extremity loss below the knee and above the ankle

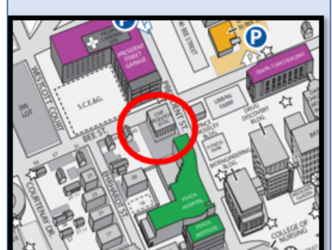
2) Ability to walk with lower extremity prosthesis without external assistive devices

3) Ability to stand without assistance of external devices (canes/crutches/assistive devices)

4) Age 18-89



All research activities are located on the campus of the Medical University of South Carolina in downtown Charleston.



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